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(54) Title: 87 HUMAN SECRETED PROTEINS

(57) Abstract

The present invention relates to 87 novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

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WO 98/42738 PCT/US98/05311

87 Human Secreted Proteins

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Field of the Invention

This invention relates to newly identified polynucleotides and the polypeptides encoded by these polynucleotides, uses of such polynucleotides and polypeptides, and their production.

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Background of the Invention

Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eucaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or organelle, contains different proteins essential for the function of the organelle. The cell uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

Despite the great progress made in recent years, only a small number of genes encoding human secreted proteins have been identified. These secreted proteins include the commercially valuable human insulin, interferon, Factor VIII, human growth hormone, tissue plasminogen activator, and erythropoeitin. Thus, in light of the pervasive role of secreted proteins in human physiology, a need exists for identifying and characterizing novel human secreted proteins and the genes that encode them. This knowledge will allow one to detect, to treat, and to prevent medical disorders by using secreted proteins or the genes that encode them.

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Summary of the Invention

The present invention relates to novel polynucleotides and the encoded polypeptides. Moreover, the present invention relates to vectors, host cells, antibodies, and recombinant methods for producing the polypeptides and polynucleotides. Also provided are diagnostic methods for detecting disorders related to the polypeptides, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying binding partners of the polypeptides.

Detailed Description

Definitions

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide.

In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X or the cDNA contained within the clone deposited with the ATCC. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, with or without the signal sequence, the secreted protein coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having the translated amino acid sequence generated from the polynucleotide as broadly defined.

In the present invention, the full length sequence identified as SEQ ID NO:X was often generated by overlapping sequences contained in multiple clones (contig

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analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X was deposited with the American Type Culture Collection ("ATCC"). As shown in Table 1, each clone is identified by a cDNA Clone ID (Identifier) and the ATCC Deposit Number. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposit was made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, the complement thereof, or the cDNA within the clone deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42° C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and $20~\mu g/ml$ denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65°C.

Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH₂PO₄; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50°C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA+ sequences (such as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a

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complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone).

The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single-and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

The polypeptide of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine,

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formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

"SEQ ID NO:X" refers to a polynucleotide sequence while "SEQ ID NO:Y" refers to a polypeptide sequence, both sequences identified by an integer specified in Table 1.

"A polypeptide having biological activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention.)

25 Polynucleotides and Polypeptides of the Invention

FEATURES OF PROTEIN ENCODED BY GENE NO: 1

The translation product of this gene shares sequence homology with nucleolin, which is thought to be important in macromolecule binding, as well as some membrane proteins. Preferred polypeptide fragments comprise the amino acid sequence: DPEAADSGEPQNKRTPDLPEEEYVKEEIQENEEAVKKMLVEATREFEEVVVDES (SEQ ID NO:239); QKLKRKAEEDPEAADSGEPQNKRTPDLPEEEYVKEEIQENEE AVKKMLVEATREFEEVVVDES (SEQ ID NO:240); KAMEKSSLTQHSWQSLKDR YLKHLRGQEHKYLLGDAPVSPSSQKLKRKAEEDPEAADSGEPQNKRTPDLPEE EYVKEEIQENEEAVKKMLVEATREFEEVVVDESPPDFEIHI (SEQ ID NO:241). Also preferred are the polynucleotide fragments encoding these polypeptide fragments.

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This gene maps to chromosome 16, and therefore can be used as a marker in linkage analysis for chromosome 16.

This gene is expressed primarily in brain and kidney and to a lesser extent in wide range of tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cell-cell interaction or cell-matrix interaction. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain and kidney, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of the nervous system, and kidney, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:125 as residues: Met-1 to Trp-10.

The tissue distribution and homology to nucleolin indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment/diagnosis of diseases involving cell-cell interaction or cell-extracellular matrix interaction.

FEATURES OF PROTEIN ENCODED BY GENE NO: 2

The translation product of this gene shares sequence homology with a porcine zona pellucida protein ZPDS.1711. (See Accession No. R39356.) These two proteins have weak homology with *Drosophila* commissureless and metal homeostasis proteins which are thought to be important in controlling growth cone guidance across the CNS midline and protecting cells against reactive oxygen toxicity. thus, based on homology, it is likely that this gene also be involved in development. Preferred polypeptide fragments comprise the amino acid sequence: LPSYDEAERTKAEATIPLVPGRDEDF VGRDDFDDADQLRIGNDGIFMLTFFMAFLFNWIGFFLSFCLTTSAAGRYGAISG FGLSLIKWILIVRFSTYFPGYFDGQYWLWWVFLVLGFLLFLRGFINYAKVRKM PETFSNLPRTRVLFI (SEQ ID NO:242); and/or AGRYGAISGFGLSLIKWILIVRFS (SEQ ID NO:243). Also preferred are polynucleotide fragments encoding these polypeptide fragments. This gene maps to chromosome 5, and therefore can be used in linkage analysis as a marker for chromosome 5.

This gene is expressed primarily in kidney, adrenal gland, brain and to a lesser extent in wide range of tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, fertilization control or tissue damages by metabolites or other toxic agents. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and urosecretion system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., kidney, adrenal gland, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to zona pellucida protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for fertility control such as controceptive development. The homology with metal homeostasis and commissureless genes indicates the gene's function in spermatozoa guidance and protection. It would also be useful for the treatment/diagnosis of tissue damages caused by toxic metabolites and other agents since the gene product is also expressed in urosecretive tissues.

25 FEATURES OF PROTEIN ENCODED BY GENE NO: 3

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This gene is expressed primarily in liver and to a lesser extent in placenta. Preferred polypeptide fragments comprise the amino acid sequence: MKHLSAWNFT KLTFLQLWEI FEGSVENCQTLTSYSKLQIKYTFSRGSTFYI (SEQ ID NO:244). Also preferred are polynucleotide fragments encoding these polypeptide fragments.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, digestive and nutrient transport/utilization disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive and

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circulatory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., liver, and placenta, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in liver and placenta indicates that the protein product is either an extracellular enzyme or a molecule carrier. Therefore, polynucleotides and polypeptides corresponding to this gene are useful for diagnosis/treatment of digestive and nutrient transport/utilization disorders, including malabsorption and malnutrition.

FEATURES OF PROTEIN ENCODED BY GENE NO: 4

This gene shares homology with the sap47 gene of Drosophila melanogaster, a gene which codes for a conserved neuronal protein associated with synaptic terminals. (See Mol. Brain Res. 32:45-54 (1995); see also, Accession No. 929571.) Thus, based on homology, the gene of the present invention also should be associated with synaptic terminals. Preferred polypeptide fragments comprise the amino acid sequence: FSSDFRTSPWESRRVESKATSARCGLWGSGPRRRPASGMFRGLSSWLGLQQP VAGGGOPNGDAPPEQPSETVAESAEEELQQAGDQELLHQAKDFGNYLFNFASA ATKKITESVAETAOTIKKSVEEGKIDGIIDKTIIGDFQKEQKKFVEEQHTKKSEA AVPPWVDTNDEETIQQQILALSADKRNFLRDPPAGVQFNFDFDQMYPVALVML (SEO ID NO:245); MRFALVPKLVKEEVFWRNYFYRVSLIKQSAQLTALAAQQQA AGKGGEEQ (SEQ ID NO:246); STSPGVSEFVSDAFDACNLNQEDLRKEMEQL VLDKKQEETAVLEEDSADWEKELQQELQEYEVVTESEKRDENWDK (SEQ ID NO:247); SPWESRRVESKATSARCGLWGSGPRRRPASGMFRGLSSWLGLQQ PVAGGGQPNGDAPPEQPS (SEQ ID NO:248); PVAGGGQPNGDAPPEQPSETV ESAEELQQAGDQELLHQAKDFGNYLFNFASAATKKITESVAE (SEQ ID NO: 249); and/or FQKEQKKFVEEQHTKKSEAAVPPWVDTNDEETIQQQILALSADKR NFLRDPPAGVQFNFDFDQMYPVALVML (SEQ ID NO:250). Also preferred are polynucleotide fragments encoding these polypeptide fragments.

This gene is expressed primarily in kidney pyramids and to a lesser extent in lung and other tissues of various types. This gene fluxes calcium in human aortic smooth muscle cells, and therefore is involved in signal transduction.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are

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not limited to, renal and nervous disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the kidney and/or nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., kidney, lung, brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in kidney and lung and homology with sap47 indicates that the protein product has regulatory or direct functions in molecular exchange with body fluids and nervous system signaling. Polynucleotides and polypeptides corresponding to this gene are useful for treatment of disorders in kidney and nervous system.

FEATURES OF PROTEIN ENCODED BY GENE NO: 5

The translation product of this gene shares sequence homology with the mouse Ly-9.2 antigen which is thought to be an important cell surface marker in lymphoids, myeloids and hematopoietic progenitors. (See Accession No. gil198932.) Preferred polypeptide fragments comprise the amino acid sequence: PFICVARNPVSRNFSSPI LARKLCEGAA (SEQ ID NO:251); and/or KEDPANTVYSTVEIPKKMENPHSLLT MPDTPRL (SEQ ID NO:252). Also preferred are polynucleotide fragments encoding these polypeptide fragments. Based on homology, it is likely that this gene is also a cell surface marker, involved in hematopoiesis.

This gene is expressed primarily in activated macrophages, monocytes and T-cells and to a lesser extent in spleen and bone marrow.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune and hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., blood cells, and bone marrow, and cancerous and wounded

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tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:129 as residues: Lys-26 to Tyr-33, Arg-44 to Ile-49, Ser-53 to Lys-71, Lys-86 to Pro-91.

The tissue distribution and homology to Ly-9.2 surface immunoglobulin family indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis of immune and hematopoietic disorders. Polypeptides and polynucleotides corresponding to this gene are also be used as a marker for leukemia or a modulator of the functions of the cells of macrophage/monocyte or T-cell types.

FEATURES OF PROTEIN ENCODED BY GENE NO: 6

The translation product of this gene shares sequence homology with the *Drosophila* glutactin gene which is thought to be important in cell-cell interaction or cell-extracellular matrix contact.

This gene is expressed primarily in colon tissue, aorta endothelial cells and to a lesser extent in skin, breast tissue and T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of these tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, diseases of the gastrointestinal tract, vascular system or T-cell development. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive system, cardiovascular system, and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., colon, cardiovascular tissue, skin, mammary tissue, and blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to glutactin indicates that polynucleotides and polypeptides corresponding to this gene are useful for the development and maintenance of the integrity of the basal membrane in the gastrointestinal tract and

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cardiovascular system. The expression in T-cells also indicate the protein may be involved in T-cell adhesion, cell-cell interaction and development.

FEATURES OF PROTEIN ENCODED BY GENE NO: 7

The translation product of this gene shares sequence homology with MURF4 protein, an ATPase homolog, which is thought to be important in ATP hydrolysis.

This gene is expressed primarily in breast tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, breast cancer and non-neoplastic breast diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the breast tissue, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., mammary tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to MURF4 gene indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of neoplastic or non-neoplastic breast diseases because ATPase like protein may be involved in changed metabolic states of the breast.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 8

This gene shares homology to the alcohol dehydrogenase gene. Preferred polypeptide fragments comprise comprise the amino acid sequence: ASAVLLDLPNSG GEAQAKKLGNNCVFAPADVTSEKDVQTALALAKGKFGRVDVAVNCAGIAVAS KTYNLKKGQTHTLEDFQRVLDVNLMGTFNVIRLVAGEMGQNEPDQGGQRGVI INTASVAAFEGQVGQAAYSASKGGIVGMTLPIARDLAPIGIRVMTIAPGLFGTPL LTSLPEKVCNFLASQVPFPSRLGDPAEYAHLVQAIIENPFLNGEVIRLDGAIRMQ P (SEQ ID NO:253); and/or SVAAFEGQVGQAAYSASKGGIVGMTLPIA (SEQ ID NO:254). Polynucleotides encoding these fragements are also encompassed by the invention. Other groups have also recently cloned this gene, recognizing its homology to alcohol dehydrogenase. (See Accession No. 1778355.) Moreover, a second group

recently cloned the mouse homologue of this gene. (See Accession No. 2078284.) They found that the mouse homologue binds to amyloid beta-peptide and mediates neurotoxicity in Alzheimer's disease, calling the protein ERAB. This gene maps to chromosome X, and therefore can be used in linkage analysis as a marker for chromosome X. Therefore, mutations in the translated product of this gene may be involved in Alzheimer's disease in humans, as well as other sex linked diseases. This gene can be used as a diagnostic marker for these diseases.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:132 as residues: Arg-45 to Ser-53.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 9

The translation product of this gene shares week sequence homology with rat N-methyl-D-aspartate receptor subunit and other proline-rich proteins which are thought to be important in neurotransmission or protein-protein intereaction.

This gene is expressed primarily in synovial hypoxia and to a lesser extent in ovary, senescent cells and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, synovial hypoxia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the synovia and brain, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., synovial tissue, ovary and other reproductive tissue, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in synovial hypoxia and nerve tissues, and homology to N-methyl-D-aspartate receptor subunit and other proline-rich proteins indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of synovial hypoxia and other synovial disorders.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 10

This gene is expressed primarily in prostate and to a lesser extent in placenta and ovary.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, male and female infertility, cancer, and other hyperproliferative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system and neoplasia, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., prostate, placenta, ovary and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:134 as residues: Pro-17 to Met-23, Ala-30 to Trp-38, Ile-49 to Trp-54, Lys-68 to Gly-74, Thr-93 to Gly-99, Met-126 to Glu-132, Gly-173 to Ser-178, Lys-205 to Tyr-214.

The tissue distribution of this gene in the prostate, placenta and ovary indicates that this gene product is useful for treatment/diagnosis of male or female infertility, endocrine disorders, fetal deficiencies, ovarian failure, amenorrhea, ovarian cancer, benign prostate hyperplasia, prostate cancer, and other forms of cancer of the reproductive system.

FEATURES OF PROTEIN ENCODED BY GENE NO: 11

This gene is expressed primarily in the thyroid and to a lesser extent in the pineal gland. This gene maps to chromosome 10, and therefore can be used as a marker in linkage analysis for chromosome 10. Preferred polypeptide fragments comprise the amino acid sequence: HPIEWAINAATLSQFY (SEQ ID NO:256); CWIKYCLTLMQN AQLSMQDNIG (SEQ ID NO:257); KVSYLRPLDFEEARELFLLGQHYVF (SEQ ID NO:258); MERRCKMHKRXIAMLEPLTVDLNPQ (SEQ ID NO:259); and/or SHIV KKINNLNKSALKY YQLFLD (SEQ ID NO:260). Also preferred are polynucleotides encoding these polypeptide fragments.

Therefore, polynucleotides and polypeptides of the invention are useful as

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reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune, thyroid and pineal gland disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., thyroid and pineal gland, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:135 as residues: Ser-2 to Ser-8, Thr-38 to Arg-44.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating/detecting immune disorders such as arthritis, asthma, immune deficiency diseases (e.g., AIDS), and leukemia, as well as treating/detecting thymus disorders (e.g., Graves Disease, lymphocytic thyroiditis, hyperthyroidism, and hypothyroidism), and treating/detecting pineal gland disorders (e.g., circadian rhythm disturbances associated with shift work, jet lag, blindness, insomnia and old age).

FEATURES OF PROTEIN ENCODED BY GENE NO: 12

This gene is expressed primarily in lung and tonsils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, pulmonary or immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the pulmonary and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., pulmonary tissue, and tonsils, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily

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fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:136 as residues: Glu-28 to Gly-49.

The tissue distribution of this gene only in lung indicates that it could play a role in the treatment/detection of lung lymphoma or sarcoma formation, pulmonary edema and embolism, bronchitis and cystic fibrosis. Its expression in tonsils indicates a potential role in the treatment/detection of immune disorders such as arthritis, asthma, immune deficiency diseases (e.g., AIDS), and leukemia, in addition to the treatment/detection of tonsillitis.

10 FEATURES OF PROTEIN ENCODED BY GENE NO: 13

This gene is expressed primarily in lymphoid, myeloid and erythroid cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, hematopoietic and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., blood cells, myeloid cells, and bone marrow, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The predominant tissue distribution of this gene in hematopoietic cell types indicates that the gene could be important for the treatment or detection of immune or hematopoietic disorders including arthritis, asthma, immunodeficiency diseases and leukemia. Preferred embodiments of the present invention are polypeptide fragments comprising the amino acid sequence: FTHLSTCLLSLLLVRMSGFLLLARASPSI CALDSSCFVEYCSSYSSSCFLHQHFPSLLDHLCQ (SEQ ID NO:261); or FLLL ARASPSICALDSSCFVQEY (SEQ ID NO:262). Also preferred are polynucleotide fragments encoding these polypeptide fragments.

FEATURES OF PROTEIN ENCODED BY GENE NO: 14

This gene is homologous to the *Drosophila Regena* (Rga) gene. (See Accession No. 1658504.) This *Drosophila* gene is thought to be a homolog of the global negative

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transcriptional regulator NOT2 (CDC36) from yeast, which modifies gene expression and suppresses position effect variegation. Preferred polypeptide fragments comprise the amino acid sequence: PDGRVTNIPQGMVTDQFGMIGLLTFIRAAETDPGMVHL ALGSDLTTLGLNLNS (SEQ ID NO:263); VHLALGSDLTTLGLNLNSPENLYP (SEQ ID NO:265); EDLLFYLYYMNGGDVLQLLAAVELFNRDWRYHKEERVWI TR (SEQ ID NO:264); and/or HNEDFPALPGS (SEQ ID NO:266).

This gene is expressed primarily in placenta and to a lesser extent in infant brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, neurodegenerative and developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neurological system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., placenta, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:138 as residues: Leu-9 to Tyr-15, Asp-34 to Gln-46, Pro-51 to Asp-57, Gly-88 to Thr-104, Thr-123 to Ser-128.

The tissue distribution of this gene indicates that it could be used in the detection and/or treatment of neurological disorders such as Such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, and panic disorder.

30 FEATURES OF PROTEIN ENCODED BY GENE NO: 15

This gene is expressed primarily in adrenal gland tumor and osteoclastoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, endocrine and bone disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for

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differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system and in bone, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., adrenal gland, and bone, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:139 as residues: Ile-52 to Trp-57.

The tissue distribution of this gene indicates that it may be involved in the treatment and/or detection of adrenal gland tumors, osteosarcomas, endocrine disorders and bone disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 16

The translation product of this gene shares sequence homology with the FK506 binding protein, a protein which plays an important role in immunosupression. (See Accession No. M75099.) Specifically, a 12-kDa FK506-binding protein (FKBP-12) is a cytosolic receptor for the immunosuppressants FK506 and rapamycin. (See, Proc. Natl. Acad. Sci. 88: 6677-6681 (1991).) Thus, based on homology, it is likely that this gene also has immunosuppression activity. Preferred polypeptides comprise the amino acid sequence: GRIIDTSLTRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRAIIPSH LAYGKRGFPPSVPADAVVQYDVELIALIR (SEQ ID NO:267); and/or IHYTGSLV DGR IIDTS (SEQ ID NO:268). Also preferred are the polynucleotide fragments encoding these polypeptides.

This gene is expressed primarily in melanocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cancer and other hyperproliferative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and cancer, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., melanocytes, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to

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the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:140 as residues: Ala-118 to Phe-124, Arg-178 to Lys-201.

The tissue distribution and homology to the FK506 binding proteins which are believed to a role in immunosupression mediated by the immunosupressant drugs rapamycin and cyclosporin, indicates that this gene could serve as a novel target for the identification of novel immunosupressant drugs.

10 FEATURES OF PROTEIN ENCODED BY GENE NO: 17

The translation product of this gene shares sequence homology with the rat calcium-activated potassium channel rSK3, which is thought to be important in regulating vascular tone. (See Accession No. gil2564072, gil1575663, and gil1575661.) Although homologous to these proteins, this gene contains an 18 amino acid insert, not previously identified in the homologs. Preferred polypeptide fragments comprise the amino acid sequence: CESPESPAQPSGSSLPAWYH (SEQ ID NO:269). Also preferred are the polynucleotide fragments encoding these polypeptides.

This gene is expressed primarily in B-cells, frontal cortex and endothelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cardiovascular (hyper/hypotension, asthma, pulmonary edema, pneumonia, heart disease, restenosis, atherosclerosis, stoke, angina and thrombosis) and neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular and nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., blood cells, brain and other tissue of the nervous system, and endothelium, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:141 as residues: Glu-72 to Gly-82, His-90 to Val-95, Gln-168 to Lys-174, Val-202 to Ser-212.

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The tissue distribution and homology to calcium-activated potassium channels indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of vascular disorders (hyper/hypotension, athesma, pulmonary edema, pneumonia, heart disease, restenosis, atherosclerosis, stoke, angina and thrombosis).

FEATURES OF PROTEIN ENCODED BY GENE NO: 18

This gene is expressed primarily in smooth muscle and to a lesser extent in brain (amygdala, corpus colosum, hippocampus).

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cardiovascular (hypertension, heart disease, athesma, pulmonary edema, restenosis, atherosclerosis, stoke, angina, thrombosis, and wound healing), and neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular and neurological systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., smooth muscle, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:142 as residues: Lys-43 to Arg-49, Tyr-58 to Glu-65.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of cadiovascular disorders (hypertension, heart disease, athesma, pulmonary edema, restenosis, atherosclerosis, stoke, angina, thrombosis, and wound healing). Expression in brain indicates a role in the treatment and diagnosis of behavioral or neurological disorders, such as depression, schizophrenia, Alzheimer's disease, mania, dementia, paranoia, and addictive behavior.

35 FEATURES OF PROTEIN ENCODED BY GENE NO: 19

This gene is expressed primarily in T-cells (Jurkats, resting, activated, and

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anergic T-cells), endothelial cells, pineal gland, and to a lesser extent in a variety of other tissues and cell types. Preferred polypeptide fragments comprise the amino acid sequence: EEAGAGRRCSHGGARPAGLGNEGLGLGGDPDHTDTGSRSKQRINN WKESKHKVIMASASARGNQDKDAHFPPPSKQSLLFCPKSKLHIHRAEISK (SEQ ID NO:270); and/or SKQRINNWKESKHKVIMASASAR (SEQ ID NO:271). Also preferred are the polynucleotide fragments encoding these polypepides.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, inflammation, immune and cardiovascular disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, neurological and vascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other blood cells, endothelial cells, and pineal gland, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:143 as residues: Phe-71 to Arg-76, Pro-82 to His-87, Glu-103 to Ala-111.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders including: leukemias, lymphomas, auto-immune, immuno-supressive (e.g. transplantation) and immunodeficiencies (e.g. AIDS) and hematopoietic disorders. In addition, expression in the pineal gland might suggest a role in the diagnosis of specific brain tumors and treatment of neurological disorders. Endothelial cell expression might suggest a role in cadiovascular or respiratory/pulmonary disorders or infections (athesma, pulmonary edema, pneumonia).

FEATURES OF PROTEIN ENCODED BY GENE NO: 20

This gene is expressed primarily in brain and embryo and to a lesser extent in leukocytes. This gene maps to chromosome 15, and therefore can be used as a marker in linkage analysis to chromosome 15.

Therefore, polynucleotides and polypeptides of the invention are useful as

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reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, developmental and neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:144 as residues: Met-1 to Gly-8.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of immune disorders including: leukemias, lymphomas, auto-immune, immuno-supressive (e.g. transplantation) and immunodeficiencies (e.g. AIDS) and hematopoietic disorders. The expression in the brain -- and in particular the fetal brain -- would suggest a possible role in the treatment and diagnosis of developmental and neurodegenerative diseases of the brain and nervous system (depression, schizophrenia, Alzheimer's disease, mania, dementia, paranoia, and addictive behavior).

FEATURES OF PROTEIN ENCODED BY GENE NO: 21

This gene is expressed primarily in brain, kidney, lung, liver, spleen, and a variety of leukocytes (especially T-cells) and to a lesser extent in a variety of other tissues and cell types.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, leukemias, lymphomas, autoimmune, immunosuppressive, and immunodeficiencies, hematopoietic disorders, as well as renal disorders, and neoplasms. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal, pulmonary, immune, and central nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g.,

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brain and other tissue of the nervous system, kidney, pulmonary tissue, liver, spleen, and blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of renal conditions, such as acture renal failure, kidney fibrosis, and kidney tubule regeneration. The expression in leukocytes and other immune tissues indicates a role in immune disorders including: leukemias, lymphomas, auto-immune, immuno-supressive (e.g. transplantation) and immunodeficiencies (e.g. AIDS) and hematopoietic disorders. The expression in the brain -- and in particular the fetal brain -- indicates a possible role in the treatment and diagnosis of developmental and neurodegenerative diseases of the brain and nervous system (depression, schizophrenia, Alzheimer's disease, mania, dementia, paranoia, and addictive behavior).

FEATURES OF PROTEIN ENCODED BY GENE NO: 22

This gene is expressed primarily in skin (fetal epithelium, keratinocytes and skin). This gene also maps to chromosome 19, and therefore can be used in linkage analysis as a marker for chromosome 19.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, skin cancers (e.g., melanomas), eczema, psoriasis or other disorders of the skin. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., skin and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:146 as residues: Pro-28 to Glu-35, Ser-39 to Phe-44, Ala-94 to Gln-99.

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The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of skin cancers (e.g., melanomas), eczema, psoriasis or other disorders of the skin.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 23

This gene maps to chromosome 11. Another group recently isolated this same gene, associating the sequence to the region thought to harbor the gene involved in Multiple Endocrine Neoplasia Type 1, or MEN 1. (See Accession No. 2529721 and Genome Res. 7(7), 725-735 (1997), incorporated herein by reference in its entirety.) Preferred polypeptide fragments comprise the amino acid sequence: LFHWACLNERA AQLPRNTAXAGYQCPSCNGPS (SEQ ID NO:272).

This gene is expressed primarily in epididymus, pineal gland, T-cells, as well as fetal epithelium, lung and kidney.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune, metabolic mediated disorders, and MEN. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, renal, neurological and pulmonary systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., epididymus and other reproductive tissue, pineal gland, T-cells and other blood cells, epithelium, lung, and kidney, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of developmental deficiencies or abnormalities as well as a host of different disorders which arise as a result of conditions in the indicated tissues or cell types. An area of particular interest is in the treatment and diagnosis of immune disorders including: leukemias, lymphomas, auto-immune, immuno-supressive (e.g. transplantation) and immunodeficiencies (e.g. AIDS) and hematopoietic disorders. The expression in the brain, and in particular the fetal brain, would suggest a possible role in the treatment and diagnosis of

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developmental and neurodegenerative diseases of the brain and nervous system (depression, schizophrenia, Alzheimer's disease, mania, dementia, paranoia, and addictive behavior). Respiratory/pulmonary disorders, such as athesma, pulmonary edema are also potential therapeutic areas, as well as renal conditions such as acute renal failure, kidney fibrosis and kidney tubule regeneration. Moreover, this gene can be used in the treatment and/or detection of MEN I.

FEATURES OF PROTEIN ENCODED BY GENE NO: 24

This gene is expressed primarily in fetal spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, leukemia, lymphoma, AIDS, hematopoeitic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., spleen and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of immune disorders including: leukemias, lymphomas, auto-immune, immuno-supressive (e.g. transplantation) and immunodeficiencies (e.g. AIDS) and hematopoietic disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 25

A closely related homolog of this gene was recently cloned by another group, calling the gene CDO, an oncogene-, serum-, and anchorage-regulated member of the Ig/fibronectin type III repeat family. (See Accession No. 2406628, and J. Cell Biol. 138(1): 203-213 (1997), herein incorporated by reference in its entirety.) Preferred polypeptide fragments comprise the amino acid sequence: FYTYYRPTDSDNDSDYKK DMVEGDKYWHSISHLQPETSYDIKMQCFNEGGESEFSNVMICETKARKSSGQP GRLPPPTLAPPQPPLPETIERPVGTGAMVARSSDLPYLIVGVVLGSIVLIIVTFIPF CLWRAWSKQKHTTDLGFPRSALPPSCPYTMVPLGGLPGHQAVDSPTSVASVD

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GPVLM (SEQ ID NO:273); or YIYYRPTDSDNDSDYKKDMVEGDKYWHSISHLQ PETSYDIKMQCFNEGGESEFSNVMICETKARKS (SEQ ID NO:274).

This gene is expressed primarily in fetal lung and kidney, human embryo and osteoclastoma stromal cells and to a lesser extent in a variety of other tissues and cell types.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, developmental disorders and cancers, as well as pulmonary and renal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the respiratory/pulmonary, skeletal and renal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., lung, kidney, embryonic tissue, and bone cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:149 as residues: Thr-5 to Pro-18, Ala-76 to Thr-84.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of: osteoperosis, fracture, osteosarcoma, ossification, and osteonecrosis, as well as respiratory/pulmonary disorders, such as athesma, pulmonary edema, and renal conditions such as acute renal failure, kidney fibrosis and kidney tubule regeneration.

FEATURES OF PROTEIN ENCODED BY GENE NO: 26

This gene is homologous to the HIV envelope glycoprotein. (See Accession No. 2641463.) Preferred polypeptide fragments comprise the amino acid sequence: NVRALLHRMPEPPKINTAKFNNNKRKNLSL (SEQ ID NO:275).

This gene is expressed primarily in pineal gland and skin, and to a lesser extent in lung.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are

not limited to, neurological and behavior disorders; respiratory/pulmonary disorders, such as athesma, pulmonary edema; skin conditions such as eczema, psoriasis, acne and skin cancer, as well as AIDS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous and respiratory systems, as well as skin and AIDS, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., blood cells, pineal gland, epidermis, and pulmonary tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:150 as residues: Gln-15 to Gln-20.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of conditions which affect the above tissues, such as: skin cancer, eczema, psoriasis, acne, athesma, pulmonary edema, neuro-degenerative or developmental disorders such as Alzheimer's, depression, schizophrenia, dementia, and AIDS.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 27

Preferred polypeptide encoded by this gene comprise the following amino acid sequence: NTNQREALQYAKNFQPFALNHQKDIQVLMGSLVYLRQGIENSPYVHL LDANQWADICDIFTRDACALLGLSVESPLSVSFSAGCVALPALINIKAVIEQRQC TGVWNQKDELPIEVDLGKKCWYHSIFACPILRQQTTDNNPPMKLVCGHIISRD ALNKMFNGSKLKCPYCPMEQSPGDAKQIFF (SEQ ID NO:276). Polynucleotides encoding such polypeptides are also provided as are complementary polynucleotides thereto.

This gene is expressed primarily in liver (adult and fetal) and spleen tissue, and to a lesser extent in placenta, T helper cells, kidney tumor, ovarian tumor, melanocytes and fetal heart.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune and developmental diseases and disorders and liver diseases such as liver cancer. Similarly, polypeptides and antibodies directed to these

polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, circulatory and hematopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., liver, spleen, placenta, blood cells, kidney, ovary and other reproductive tissue, melanocytes, and heart, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that the protein products of this gene are useful for study, diagnosis and treatment of growth, hematopoietic and immune system disorders particularly related to the liver.

FEATURES OF PROTEIN ENCODED BY GENE NO: 28

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The translation product of this gene shares sequence homology with prostaglandin transporter which is thought to be important in metabolic and endocrine disorders. See, for example, Gastroenterology Oct:109(4):1274-1282 (1995). Preferred polypeptides encoded by this gene comprise the following amino acid sequence: SYLSACFAGCNSTNLTGCACLTTVPAENATVVPGKCPSPGCQEAFLTFLCVMCI CSLIGAMARHP (SEQ ID NO:277); and/or PSVIILIRTVSPELKSYALGVLFLLLRL LGFIPPPLIFGAGIDSTCLFWSTFCGEQGACVLYDNVVYRYLYVSIAIALKSFAFI (SEQ ID NO:278).

This gene is expressed primarily in hematopoietic and brain tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, metabolic, immune and endocrine diseases and disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the metabolic, immune and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., endocrine tissue, hematopoietic tissue, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to

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the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to prostaglandin (and anion) transporter indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of endocrine, metabolic, immune and kidney disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 29

This gene is expressed primarily in early stage human lung.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, growth and respiratory disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developmental and respiratory systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., pulmonary tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:153 as residues: Val-50 to Trp-55.

The tissue distribution indicates that the protein products of this gene are useful for study, diagnosis and treatment of respiratory and growth diseases and disorders.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 30

The translation product of this gene shares sequence homology with human DNA helicase which is thought to be important in accurate and complete DNA replication in creation of new cells. Preferred polypeptides encoded by this gene comprise the following amino acid sequence: QSLFTRFVRVGVPTVDLDAQGRARA SLCXXYNWRYKNLGNLPHVQLLPEFSTANAGLLYDFQLINVEDFQGVGESEPN PYFYQNLGEAEYVVALFMYMCLLGYPADKISILTTYNGQKHLIRDIINRRCGNN PLIGRPNKVTTVDRFQGQQNDYILLSLVRTRAVGHLRDVRRLVVAMSRAR (SEQ ID NO:279); and/or LVKEAKIIAMTCTHAALKRHDLVKLGFKYDNILMEE AAQILEIETFIPLLLQNPQDGFSRLKRWIMIGDHHQLPPVI (SEQ ID NO:280).

This gene is expressed primarily in testes tumor and to a lesser extent in adrenal

gland tumor and placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cancers and endocrine/growth disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine, developmental, and reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., testes and other reproductive tissue, adrenal gland, and placenta, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to DNA helicase indicates that the protein products of this gene are useful for study, treatment, and diagnosis of many cancer types, including testicular cancer; as well as disorders involving endocrine function and normal growth and development.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 31

The translation product of this gene shares sequence homology with BID-apoptotic death gene (mouse), Genbank accession no. PID g1669514, which is thought to be important in programmed cell death.

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This gene is expressed primarily in jurkat membrane bound polysomes and activated neutrophils and to a lesser extent in endothelial cells and human cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cancers and other proliferative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., blood cells, endothelium, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma,

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urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:155 as residues: Glu-4 to Leu-11, Cys-28 to Arg-35, Gln-50 to His-66, Glu-73 to Gln-79, Gly-94 to Ser-100, Arg-114 to Asp-126, Pro-139 to Lys-146.

The tissue distribution and homology to BID-apoptotic death gene indicates that the protein products of this gene are useful for study of cell death, and treatment and diagnosis of proliferative disorders and cancers. Apoptosis - programmed cell death - is a physiological mechanism involved in the deletion of peripheral T lymphocytes of the immune system, and its dysregulation can lead to a number of different pathogenic processes. Diseases associated with increased cell survival, or the inhibition of apoptosis, include cancers (such as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, such as breast cancer, prostrate cancer, Kaposiís sarcoma and ovarian cancer); autoimmune disorders (such as systemic lupus erythematosus and immune-related glomerulonephritis rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation; graft vs. host disease, acute graft rejection, and chronic graft rejection. Diseases associated with increased apoptosis include AIDS; neurodegenerative disorders (such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Retinitis pigmentosa, Cerebellar degeneration); myelodysplastic syndromes (such as aplastic anemia), ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion injury), toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia. Thus, the invention provides a method of enhancing apoptosis in an individual by treating the individual with a polypeptide encoded by this gene.

FEATURES OF PROTEIN ENCODED BY GENE NO: 32

The translation product of this gene shares sequence homology with human fructose transporter which is thought to be important in normal metabolic function and activity.

This gene is expressed primarily in T-cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are

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not limited to, leukemia and other cancers, and metabolic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic, lymph and metabolic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:156 as residues: Pro-22 to Gly-48, Ser-54 to Pro-61.

The tissue distribution indicates that the protein products of this gene are useful for study of mechanisms leading to cancer, treatment and diagnosis of cancerous and pre-cancerous conditions; as well as the study and treatment of various metabolic diseases and disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 33

This gene is expressed primarily in human meningima.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, inflammation and other disorders of the CNS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the CNS and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., meningima and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:157 as residues: Asn-23 to Pro-31.

The tissue distribution indicates that the protein products of this gene are useful for study, diagnosis and treatment of disorders of the CNS and inflammatory responses.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 34

This gene is expressed primarily in activated monocytes and wound healing tissues and to a lesser extent in fetal epithelium.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune and inflammatory disorders and wound healing and tissue repair dysfunctions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, epithelial and gastrointestinal systems, and healing wounds, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., monocytes and other blood cells, and epithelium, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:158 as residues: Ala-28 to Ala-33, Gly-35 to Glu-45.

The tissue distribution indicates that the protein products of this gene are useful for diagnosis, study and treatment of immune and inflammatory disorders and wound healing dysfunctions.

25 FEATURES OF PROTEIN ENCODED BY GENE NO: 35

This gene is expressed primarily in human osteosarcoma and prostate cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, skeletal and neoplastic conditions such as bone and prostate cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and skeletal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., bone, and prostate, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial

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fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:159 as residues: Ser-14 to Gly-22, Leu-37 to Gln-43.

The tissue distribution indicates that the protein products of this gene are useful for diagnosis and treatment of skeletal disorders and cancer).

FEATURES OF PROTEIN ENCODED BY GENE NO: 36

This gene encodes a protein which is highly homologous to a protein called congenital heart disease protein 5, presumably implicated in congenital heart disease (see Genbank PID g2810996).

This gene is expressed primarily in Hodgkin's lymphoma, erythroleukemia cells, and TNF activated synovial fibroblasts, to a lesser extent in ovarian cancer, cerebellum, spleen, fetal liver and placenta and finally to a lesser extent in various other mesenchymal tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cancer, immune, hematopoietic and cardiovascular disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, hematopoietic and cardiovascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., heart and other cardiovascular tissue, lymphoid tissue, blood cells, bone marrow, ovary and other reproductive tissue, brain and other tissue of the nervous system, spleen, liver, and mesenchymal tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:160 as residues: Lys-41 to Met-49, Gln-54 to Glu-59, Glu-76 to Thr-88.

The homology of this gene and translation product to congenital heart disease protein 5 indicates a role for this protein in the diagnosis, prognosis and/or treatment of

heart disease or other cardiovascular related disorders. In addition, predominant expression in cells associated with the immune and hematopoetic system indicates a role for this protein in the treatment, diagnosis and/or prognosis of immune and autoimmune diseases, such as lupus, transplant rejection, allergic reactions, arthritis, asthma, immunodeficiency diseases, leukemia, AIDS, thymus disorders such as Graves Disease, lymphocytic thyroiditis, hyperthyroidism and hypothyroidism, graft versus host reaction, graft versus host disease, transplant rejection, myelogenous leukemia, bone marrow fibrosis, and myeloproliferative disease. The protein could also be used to enhance or protect proliferation, differentiation and functional activation of hematopoietic progenitor cells such as bone marrow cells, which could be useful for cancer patients undergoing chemotherapy or patients undergoing bone marrow transplantation. The protein may also be useful to increase the proliferation of peripheral blood leukocytes, which could be useful in the combat of a range of hematopoietic disorders including immunodeficiency diseases, leukemia, and septicemia.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 37

This gene is expressed primarily in ovarian cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, urogenital neoplasias. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., ovary and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:161 as residues: Asn-22 to Asn-27.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of ovarian and other tumors.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 38

The translation product of this gene shares sequence homology with zinc finger proteins.

This gene is expressed primarily in various fetal, cancer, and endothelial lines.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune and growth disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., fetal tissue, and endothelial cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that the protein products of this gene are useful for study, diagnosis and treatment of immune and developmental conditions and cancer.

FEATURES OF PROTEIN ENCODED BY GENE NO: 39

This gene is expressed primarily in fetal, infant, and adult brain and to a lesser extent in other brain and endocrine organs and blastomas.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, brain tumors and neurodegenerative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of the nervous system, endocrine tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the

disorder.

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The tissue distribution indicates that the protein products of this gene are useful for the study, diagnosis and treatment of brain cancer and other neurological disorders.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 40

The translation product of this gene shares sequence homology with vesicular glycoproteins and lectins. Preferred polypeptides encoded by this gene comprise the following amino acid sequence: DTYPNEEKQQERVFPXXSAMVNNGSLSYDHER DGRPTELGGCXAIVRNLHYDTFLVIRYVKRHLTIMMDIDGKHEWRDCIEVPGV RLPRGYYFGTSSITGDLSDNHDVISLKLFELTVERTPEEE (SEQ ID NO:281); and/or LKREHSLSKPYQGVGTGSSSLWNLMGNAMVMTQYIRLTPDMQSKQGA LWNRVPCFLRDWELQVHFKIHGQGKKNLHGDGLAIWYT (SEQ ID NO:282).

This gene is expressed primarily in infant brain and to a lesser extent in various normal and transformed neural, endocrine, and immune organs.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, neurological and neurodevelopmental conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and hormonal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of the nervous system, endocrine tissue, and tissue and cells of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:164 as residues: Pro-64 to Gly-71, Gly-94 to Leu-100, Thr-110 to Pro-116, Thr-135 to Arg-145, Glu-164 to Glu-171, Asp-204 to Asp-211, Arg-253 to His-261, Asn-312 to Tyr-323.

The tissue distribution indicates that the protein products of this gene are useful for the study, diagnosis and treatment of mental retardation and other neurological disorders and neoplasias.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 41

This gene displays homology to the glycosyltransferase family, which catalyze the addition of sialic acids to carbohydrate groups which are present on glycoproteins.

This gene is expressed primarily in smooth muscle and to a lesser extent in pineal gland, fetal liver, and infant brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, gastrointestinal injury, inflammatory and neurodegenerative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., smooth muscle, pineal gland, liver, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:165 as residues: Ser-12 to Trp-21, Arg-24 to Pro-32, Asp-73 to Lys-82, Lys-90 to Ala-97.

The tissue distribution indicates that the protein products of this gene are useful for the study, diagnosis and treatment of neurodegenerative and growth disorders and gastrointestinal repair.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 42

The translation product of this gene shares sequence similarity with metallothionein polypeptides. See, for example, Proc. Natl. Acad. Sci. U S A 1992 Jul 15:89(14):6333-6337. Metallothioneins are believed to inhibit neuronal survival among other biological functions. Based on the sequence similarity (especially the conserved cysteine motifs characteristic of the metallothionein family) the translation product of this gene is expected to share certain biological activities with other members of the metallothionein polypeptide family. Preferred polypeptides encoded by this gene comprise the following amino acid sequence: PGTLQCSALHHDPGCANCSRFCRD CSPPACQC (SEQ ID NO:283).

This gene is expressed exclusively in placenta and fetal liver.

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Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, hematopoietic and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., placenta, liver, brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to metallothionien indicates that the protein products of this gene are useful for diagnosis and treatment of immune and hematopoietic system disorders and neurological diseases, especially in fetal development.

20 FEATURES OF PROTEIN ENCODED BY GENE NO: 43

Preferred polypeptides encoded by this gene comprise the following amino acid sequence: FLYDVLMXHEAVMRTHQIQLPDPEFPS (SEQ ID NO:284).

This gene is expressed primarily in T-cells and synovial tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., synovial tissue, and T-cells and other blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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The tissue distribution indicates that the protein products of this gene are useful for treatment and diagnosis of disorders of the immune system.

FEATURES OF PROTEIN ENCODED BY GENE NO: 44

The translation product of this gene shares sequence similarity with several methyltransferases (e.g., see Genbank gil1065505).

This gene is expressed primarily in ovary, thymus, infant adrenal gland, tissues of the nervous system and the hematopoietic tissue, and to a lesser extent in adipose tissue and many other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, disorders of the reproductive system, the endocrine system, the hematopoietic system and the CNS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, endocrine, CNS and reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., ovary and other reproductive tissue, thymus, adrenal gland, brain and other tissue of the nervous system, hematopoietic tissue, and adipose tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:168 as residues: Ser-3 to Gly-12, Asp-19 to Arg-31, Tyr-70 to Tyr-77, Asn-130 to Lys-140, Pro-165 to Gln-170, Pro-192 to Lys-199, Leu-216 to Glu-227, Glu-254 to Phe-281.

The tissue distribution and homology to methyltransferase indicates that the protein products of this gene are useful for diagnosis and treatment of disorders of the CNS, the hematopoietic system and reproductive organs and tissues. For example, the abundant expression in the ovary may indicate that the gene product can be used as a hormone with either systemic or reproductive functions; as growth factors for germ cell maintenance and in vitro culture; as a fertility control agent; remedy for sexual dysfunction or sex development disorders; diagnostics/treatment for ovarian tumors, such as serous adenocarcinoma, dysgerminoma, embryonal carcinoma,

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choriocarcinoma, teratoma, etc; The expression in thymus may indicate its utilities in T-cell development and thus its applications in immune related medical conditions, such as infection, allergy, immune deficiency, tissue/organ transplantation, etc.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 45

The translation product of this gene shares sequence homology with cytochrome C oxidase which is thought to be important in metabolic function of cells. This gene has now recently been published as estrogen response gene. See Genbank accession no. AB007618 and Mol. Cell. Biol. 18 (1), 442-449 (1998). See also J Immunol. Mar 1:154(5): 2384-2392 (1995), where the mouse homologue was published and implicated in siliocis.

This gene is expressed primarily in adipose tissue, kidney and fetal brain and to a lesser extent in several other tissues and organs.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, metabolic diseases involving especially adipose tissue, brain and kidney. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the CNS and vascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., adipose tissue, kidney, brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:169 as residues: Thr-5 to Ser-14.

The tissue distribution and homology to cytochrome C oxidase, estrogen response gene product and siliocis related gene product indicates that the protein products of this gene are useful for diagnosis and treatment of metabolic disorders in the CNS, adipose tissue and kidney, particularly siliocis.

FEATURES OF PROTEIN ENCODED BY GENE NO: 46

The translation product of this gene shares sequence homology with reticulocalbin. See, for example, J. Biochem. 117 (5), 1113-1119 (1995). Based on the

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• sequence similarity, the translation product of this gene is expected to share certain biological activities with reticulocalbin, e.g., Ca++ binding activities. This gene product is sometimes hereinafter referred to as "Reticulocalbin-2".

This gene is expressed primarily in breast, endothelial cells, synovial, heart and smooth muscle cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, diseases of the breast, vascular and skeletal/cardiac muscular system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the breast, vascular and skeleto-muscular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., mammary tissue, endothelial cells, synovial tissue, heart and other cardiovascular tissue, and smooth muscle, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:170 as residues: Gly-16 to Arg-32, Ala-42 to Asn-50, Glu-66 to Gln-76, Arg-85 to Gly-94, Thr-108 to Asp-115, Trp-121 to Gly-130, Leu-137 to His-144, Glu-155 to Lys-161, Asp-175 to Ser-180, Glu-209 to Gly-217, Glu-232 to Glu-237, Thr-243 to Asp-261, Glu-287 to Arg-295.

The tissue distribution indicates that the protein products of this gene are useful for diagnosis and treatment of diseases of the vascular and skeletal/cardiac muscular system. The homology of the gene with reticulocalbin indicates its biological function in regulating calcium store, a particularly important function in muscular cell types. The gene expression in the heart may indicate its utilities in diagnosis and remedy in heart failure, ischemic heart diseases, cardiomyopathy, hypertension, arrhythmia, etc. The abundant expression in the breast may indicate its applications in breast neoplasia and breast cancers, such as fibroadenoma, papillary carcinoma, ductal carcinoma, Pagetís disease, medullary carcinoma, mucinous carcinoma, tubular carcinoma, secretory carcinoma and apocrine carcinoma; juvenile hypertrophy and gynecomastia, mastitis and abscess, duct ectasia, fat necrosis and fibrocystic diseases, etc.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 47

The translation product of this gene shares weak sequence homology with H+-transporting ATP synthase which is thought to be important in cell metabolism or signal transduction.

This gene is expressed only in testis.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of some types of diseases and conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain and hematopoietic tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., testes and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Since only one out of about a million expressed sequence tag is found in testes indicates that its expression is low and selectively in testes. Since some of the genes only expressed in testes are usually expressed in brain or in certain induced hematopoietic cells/tissues, it is speculated that this gene to be expressed in brain or hematopoietic cells/tissues and is useful for diagnosis and treatment of disorders these systems.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 48

The translation product of this gene shares sequence homology with human polymeric immunoglobulin receptor (accession No.X73079) which is thought to be important in antibody recognition and immune defenses. In one embodiment, polypeptides of the invention comprise the sequence GWYWCG (SEQ ID NO:285). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in placenta and to a lesser extent in corpus callosum and fetal liver and spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are

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not limited to, disorders of the immune system, e.g. autoimmune diseases and immunodeficiency. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., placenta, liver, and spleen, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:172 as residues: Tyr-37 to Cys-49, Gly-51 to Tyr-56, Lys-88 to Trp-93, Leu-130 to Glu-136.

The tissue distribution and homology to human polymeric immunoglobulin receptor indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of immune disorders, e.g. autoimmune diseases and immunodeficiencies.

FEATURES OF PROTEIN ENCODED BY GENE NO: 49

This gene is expressed in thymus.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune disorder. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., thymus and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of immune disorders, e.g. autoimmunity and immunodeficiency.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 50

Preferred polypeptide encoded by this gene comprise the following amino acid sequence: MKVGARIRVKM,SVNKAHPVVSTHWRWPAEWPQMFLHLAQEPRTE VKSRPLGLAGFIRQDSKTRKPLEQETIMSAADTALWPYGHGNREHQENELQKY LQYKDMHLLDSGQSLGHTHTLQGSHNLTALNI (SEQ ID NO:286). Polynucleotides encoding this polypeptide are also provided as are complementary polynucleotides thereto.

This gene is expressed primarily in adrenal gland, pituitary, T helper cells, and breast cells and to a lesser extent in a wide variety of tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of the some diseases and conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., adrenal gland, pituitary, T-cells and other blood cells, and mammary tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:174 as residues: Gln-39 to Ser-47, Arg-57 to Glu-67, Tyr-82 to Gln-95.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of a wide range of disorders, such as immune and endocrine disorders.

30 FEATURES OF PROTEIN ENCODED BY GENE NO: 51

The translation product of this gene shares sequence homology with human Sop2p-like protein which is important in cytoskeleton structure. In one embodiment, polypeptides of the invention comprise the sequence SLHKNSVSQISVLSGGKAKCS QFCTTGMDGGMSIWDVKSLESALKDLKI (SEQ ID NO:287). Polynucleotides encoding this polypeptide are also encompassed by the invention. This gene maps to chromosome 7. Therefore, polynucleotides of the invention can be used in linkage

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analysis as a marker for chromosome 7.

This gene is expressed primarily in immune and hematopoietic tissues/cells and to a lesser extent in other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immunological and hematopoietic disorders and inflammation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., immune and hematopoietic tissue/cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:175 as residues: Lys-49 to Gln-54, Ala-61 to Arg-66, Lys-82 to Lys-87, Glu-126 to Val-133, His-136 to Ile-141, Glu-175 to Ser-187, Asp-286 to Leu-296, Ala-298 to Ser-310.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of immunological, hematopoietic, and inflammatory disorders, e.g, immunodeficiency, autoimmunity, inflammation.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 52

The translation product of this gene shares sequence homology with *Caenorhabditis elegans* R53.5 gene encoding a putative secreted protein without known function.

This gene is expressed primarily in endothelial cells, brain and several highly vascularized, and tumor tissues and to a lesser extent in other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, aberrant angiogensis and tumorigenesis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

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for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular and brain system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endothelial cells, brain and other tissue of the nervous system, and vascular tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:176 as residues: Thr-43 to Asn-60, Thr-106 to Phe-115, Asp-122 to Arg-133, Arg-186 to Asp-192, Leu-211 to Lys-216.

The tissue distribution and homology to a *C. elegans* secreted protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis or treatment of disorders in vascular or brain system, e.g. aberrant angiogenesis, ischemia, neurodegeneration, etc.

FEATURES OF PROTEIN ENCODED BY GENE NO: 53

In one embodiment, polypeptides of the invention comprise the sequence EASKSSHAGLDLFSVAACHRF (SEQ ID NO:288). Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in T-cells and to a lesser extent in brain. Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, lymphocytic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the lymphoid system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other blood cells, brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:177 as residues: Pro-3 to Thr-8, Arg-37 to Asp-46.

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The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis, treatment, and cure of lymphocytic disorders.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 54

The translation product of this gene shares sequence homology with secreted cartilage matrix protein, a major component of the extracellular matrix of nonarticular cartilage which is thought to be important in cartilage structure. In specific embodiments, polypeptides of the invention comprise the sequence: RCKKCTEGPI DLVFVIDGSKSLGEENFEVVKQF (SEQ ID NO:297); VTGIIDSLTISPKAARVGL LQYSTQVH (SEQ ID NO:290); TEFTLRNFNSAKDMKKAVAHMKYM (SEQ ID NO:291); GKGSMTGLALKHMFERSFTQGEGARPF (SEQ ID NO:292); STRVP RAAIVFTDGRAQDDVSEWASKAKANGITMYAVGVGKAIE (SEQ ID NO:293); EELQEIASEPTNKHLFYAEDFSTMDEISEKLKKGICEALEDS (SEQ ID NO:294); TQRLEEMTQRM (SEQ ID NO:295); PQGCPEQPLH (SEQ ID NO:296); and/or YMGKGSMTGLALKHMFERSFT (SEQ ID NO:289). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in placenta, infant brain, prostate, fetal lung and to a lesser extent in endometrium and fetal tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, abnormal placenta and pregnancy, disorder and injury in brain, prostate, and vasculature. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproduction, neuronal, and vascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., placenta, brain and other tissue of the nervous system, prostate, lung and endometrium, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to cartilage matrix protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis,

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treatment, and cure of abnormalities in placenta and pregnancy, disorder and injury in brain, prostate, and vasculature.

FEATURES OF PROTEIN ENCODED BY GENE NO: 55

The translation product of this gene is the human ortholog of bovine and hamster CII-3, a succinate-ubiquinone oxidoreductase complex II membrane-intrinsic subunit, which is thought to be important in mitochondrial electron transport chain during metabolism. In specific embodiments, the polypeptides of the invention compriseMAALLLRHVGRHCLRAHFSPQLCIRNAVPLGTTAKEEMERFWNKNIG SNRPLSPHITIYS (SEQ ID NO:298); VFPLMYHTWNGIRHLMWDLGKGLKIPQL YQSG (SEQ ID NO:299); MAALLLRHVGRHCLRAH (SEQ ID NO:300); VKSLCL GPALIHTAKFAL (SEQ ID NO:301); VFPLMYHTWNGIRHLMWDLGKGL (SEQ ID NO:302).

This gene is expressed in 8-week old early stage human.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, metabolism disorder. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the [insert system where a related disease state is likely, e.g., immune], expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis, treatment, and cure of metabolism disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 56

This gene is expressed primarily in umbilical vein endothelial cells, human ovarian tumor cells, human meningima cells, and human Jurkat membrane bound polysomes. In specific embodiments, polypeptides of the invention comprise the amino acid sequence: RVWDVRPFAPKERCVKIFQGNV (SEQ ID NO:303); HNFEKNLL

RCSWSPDGSKIAAGSADRFVYV (SEQ ID NO:304); and/or WDTTSRRILYKLPG HAGSINEVAFHPDEPI (SEQ ID NO:305). Polynucleotides encoding these polypeptides are also encompassed by the invention.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, inflammation, immune and cardiovascular disorders and urogenital neoplasias. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of these tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, neurological, urogenital, reproductive system and vascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., blood cells, cells, endothelial cells, ovary and other reproductive tissue, meningima, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:143 as residues: Phe-71 to Arg-76, Pro-82 to His-87, Glu-103 to Ala-111.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders including: leukemias, lymphomas, auto-immune, immuno-supressive (e.g. transplantation) and immunodeficiencies (e.g. AIDS) and hematopoietic disorders. In addition, expression in ovarian tumor cells suggests that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis, and treatment of ovarian tumors, and other tumors and neoplasias. Further, endothelial cell expression suggests a role in cadiovascular or respiratory/pulmonary disorders or infections (athsma, pulmonary edema, pneumonia).

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FEATURES OF PROTEIN ENCODED BY GENE NO: 57

The translation product of this gene shares sequence homology with type I collagen. In specific embodiments, the polypeptides of the invention comprise the sequence: GRIPAPAPSVPAGPDSR (SEQ ID NO:309); VRGRTVLRPGLDAEPE LSPE (SEQ ID NO:306); EQRVLERKLKKERKKEERQ (SEQ ID NO:307); ARRSG

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AELAWDYLCRWAQKHKNWRFQKTRQTWLLLHMYDSDKVPDEHFSTLLAYLE GLQGR (SEQ ID NO:255); and/or RLREAGLVAQHPP (SEQ ID NO:308). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in epididymus, prostate cell line (LNCAP), and pituitary gland; and to a lesser extent in many other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, abnormalities of the epididymus, prostate (especially prostate cancer), and pituitary gland. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive system and neuroendocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., epididymus and other reproductive tissue, prostate, and pituitary gland, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to type I collagen, indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of abnormalities of the epididymus, prostate (especially prostate cancer), and pituitary gland.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 58

This gene is expressed primarily in the frontal cortex of the brain from a schizophrenic individual.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, schizophrenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of

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the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of schizophrenia.

FEATURES OF PROTEIN ENCODED BY GENE NO: 59

The polypeptide encoded by Gene 59 is homologous to human surface 4 integral membrane protein. In specific embodiments, the polypeptides of the invention comprise the sequence: TGCVLVLSRNFVQYACFGLFGIIALQTIAYSILWDLKF LMRN (SEQ ID NO:310); SRSEGKSMFAGVPTMRESSPKQYMQLGGRVLLV LMFMTLLHFDASFFSIVQNIVG (SEQ IDNO:311); GTAEDFADQFLRVTKQYLP HVARLCLISTFLEDGIRMFQWSEQRDYIDTTWNCGYLLAS (SEQ ID NO:312); LMRNESRS (SEQ ID NO:314); ASFLLSRTSWGTA (SEQ ID NO:315); and/or ASFLLSRTSWGTALMIL (SEQ ID NO:313). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in Hodgkin's lymphoma and lung; and to a lesser extent in many other human tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, Hodgkin's lymphoma, tumors or other abnormalities of the lung. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and respiratory systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., lymphoid tissue, and pulmonary tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:183 as residues: Met-20 to Trp-27.

The tissue distribution indicates that polynucleotides and polypeptides

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corresponding to this gene are useful for diagnosis and treatment of Hodgkin's lymphoma, tumors or other abnormalities of the lung.

FEATURES OF PROTEIN ENCODED BY GENE NO: 60

This gene is expressed primarily in bone cancer and stomach cancer, and to a lesser extent in many other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, bone cancer and stomach cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the bone, and the stomach, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., bone, and stomach, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of bone cancer and stomach cancer and possibly other cancers.

FEATURES OF PROTEIN ENCODED BY GENE NO: 61

This gene is expressed primarily in epididymus, and lymph node of breast cancer, and to a lesser extent in many other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, abnormalities of the epididymus, and breast cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the epididymus and breast, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., epididymus and other reproductive tissue, lymphoid tissue, and mammary tissue, and cancerous and wounded tissues) or bodily fluids

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(e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:185 as residues: Arg-57 to Ser-65.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of abnormalities of the epididymus, and breast cancer.

10 FEATURES OF PROTEIN ENCODED BY GENE NO: 62

The translation product of this gene appears to be the human homolog of bovine NADH dehydrogenase which is thought to be important in cellular metabolism. In specific embodiments, the polypeptides of the invention comprise the amino acid sequence: SMSALTRLASFARVGGRLFRSGCARTAGDGGVRHAGGGVHIEPRY RQFPQLTRSQVFQSEFFSGLMWFWILWRFWHDSEEVLGHFPYPDPSQWTDEEL GIPPDDED (SEQ ID NO:323), or fragments thereof. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed in larynx tumor, lymph node, brain amygdala, human cardiomyopathy, and retina.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, diseases affecting cellular metabolism. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., larynx, lymphoid tissue, brain and other tissue of the nervous system, heart and cardiovascular tissue, and retina, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:208 as residues: Pro-27 to Gln-32, Arg-42 to Glu-51.

The tissue distribution and homology to NADH dehydrogenase indicates that

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polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases involving cellular metabolism.

FEATURES OF PROTEIN ENCODED BY GENE NO: 63

This gene is expressed primarily in amygdala, and to a lesser extent in many other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, abnormalities of the amygdala. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the amygdala, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., amygdala, and lymphoid tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:187 as residues: Gln-17 to Glu-29, Pro-41 to Phe-46, Ser-59 to Ile-70, Thr-97 to Leu-105.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of abnormalities of amygdala.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 64

This gene is expressed primarily in female bladder, and to a lesser extent in chronic synovitis and hemangiopericytoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, bladder cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the urinary tract, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., bladder, synovial tissue, and

vascular tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:188 as residues: Pro-2 to Gln-7, Pro-27 to Phe-34.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatments of defects of the urinary tract, especially bladder cancer.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 65

This gene is expressed primarily in fetal spleen, and to a lesser extent in hemangiopericytoma, thymus, and synovial sarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, defects of immune of hematopoietic systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune of hematopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., spleen, vascular tissue, thymus, blood cells, and synovial tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The protein product of this gene is useful for treatment of defects of the immune or hematopoietic systems, because of the gene's expression in thymus and spleen.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 66

This gene is expressed primarily in human pituitary and to a lesser extent in placenta and fetal lung.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are

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not limited to, endocrine growth disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., pituitary and other endocrine tissue, placenta, and pulmonary tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:190 as residues: Val-38 to Asn-44, Gly-53 to Ser-65.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment of growth disorders related to pituitary dysfunction.

FEATURES OF PROTEIN ENCODED BY GENE NO: 67

The translation product of this gene shares sequence homology with a *Caenorhabditis elegans* gene of unknown function. In specific embodiments, the polypeptides of the invention comprise the sequence: DPRRPNKVLRYKPPPSE CNPALDDPTP (SEQ ID NO:317); DYMNLLGMIFSMCGLMLKLKWCAWVA VYCS (SEQ ID NO:318); FISFANSRSSEDTKQMMSSF (SEQ ID NO:316); and/or MLSISAVVMSYLQNPQPMTPPW (SEQ ID NO:319). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in primary breast cancer and lymph node breast cancer and to a lesser extent in adult brain, lung cancer, colon cancer, epithelioid sarcoma, and Caco-2 cell line.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cancer and tumor tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., mammary tissue, lymphoid tissue, brain and other tissue of the nervous system, lung, colon, and

epithelium, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:191 as residues: Asn-34 to Lys-42.

The tissue distribution in a variety of cancer tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of a variety of cancer and tumor types.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 68

The translation product of this gene shares sequence homology with steroid membrane binding protein. The translation product of this gene has recently been published as progesterone binding protein. See Genbank AJ002030. Preferred polypeptides encoded by this gene comprise the following amino acid sequence: AAGDGDVKLGTLGSGSESSNDGGSESPGDAGAAAXGGGWAAAALALLTG GGE (SEQ ID NO:320).

This gene is expressed primarily in breast, and to a lesser extent in placenta and fetal tissue.

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Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, breast cancer or developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of breast or fetal tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., mammary tissue, placenta, and fetal tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:192 as residues: Pro-43 to Asp-49, Gln-54 to Pro-64, Asp-110 to Asp-118, Lys-138 to Tyr-143, Pro-150 to Asp-170.

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The tissue distribution and homology to steroid membrane binding protein and to progesterone binding protein indicates that the protein products of this gene are

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useful for treatment of breast cancers, especially those caused by estrogen and progesterone binding.

FEATURES OF PROTEIN ENCODED BY GENE NO: 69

Preferred polypeptides encoded by this gene comprise the following amino acid sequence: AADNYGIPRACRNSARSYGAAWLLLXPAGSSRVEPTQDISISDQLGG QDVPVFRNLSLLVVGVGAVFSLLFHLGTRERRRPHAXEPGEHTPLLAPATAQPL LLWKHWLREXAFYQVGILYMTTRLIVNLSQTYMAMYLTYSLHLPKKFIATIPLV MYLSGFLSSFLMKPINKCIGRN (SEQ ID NO:321).

This gene is expressed primarily in macrophage (GM-CSF treated), and to a lesser extent in monocytes and dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, inflammation and infection. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., macrophages and other blood cells, and dendritic cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that the protein products of this gene are useful for treatment of infection or inflammation or other events or defects involving the immune system.

FEATURES OF PROTEIN ENCODED BY GENE NO: 70

This gene is expressed primarily in adult brain and to a lesser extent in thyroid, 12 week old early stage human, and stromal cell TF274.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, neurological or neuro-endocrine diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

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for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous or endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., brain and other tissue of the nervous system, thyroid, and stromal cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:194 as residues: Pro-65 to Cys-71.

The tissue distribution indicates that the protein products of this gene are useful for treatment and diagnosis of neurological diseases or metabolic conditions involving the neuro-endocrine system.

15 FEATURES OF PROTEIN ENCODED BY GENE NO: 71

This gene is expressed in T-cell helper and to a lesser extent in adult brain and adult testes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, immune disorders, meningitis or reproductive problems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, neural and reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other blood cells, brain and other tissue of the nervous system, testes and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:195 as residues: Val-18 to Tyr-24, Ala-89 to Asp-99, Asp-104 to Ala-117, Leu-121 to Pro-136.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis immune and

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reproductive disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 72

The translated polypeptide of this contig has a high degree of identity with the Ob Receptor-Associated Protein deposited as GenBank Accession No. 2266638. No function has been determined for the Ob Receptor-Associated Protein, however it is expressed upon stimulation of the Ob Receptor by Leptin.

This gene is expressed in T-cells and to a lesser extent in endothelial and bone marrow cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, acute lymphoblastic leukemia, hematapoetic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematapoetic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other blood cells, endothelial cells, and bone marrow, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:196 as residues: Ser-61 to Trp-70.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of leukemia and other disorders of the primary immune system. In addition, since this gene appears to be related to the Ob Receptor-Related Protein, it is likely that this polypeptide is also involved in the Ob/Leptin signal transduction cascade. As a result, this protein may be of use in the molecular diagnosis and therapeutic intervention of obesity and related disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 73

The translation product of this contig has homology with furin, a protein thought to be a key endopeptidase in the constitutive secretory pathway. The identification and initial characterization of Furin was reported by Takahasi and

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colleagues (Biochem Biophys Res Commun 1993 Sep 15;195(2):1019-1026).

This gene is expressed in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, diseases of the immune system such as allergies, wound healing and antigen recognition. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., neutrophils and other blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment of allergies or other immune disorders since neutrophils are an important part of an allergic response. Further, since this protein appears to be related to Furin, it can be used diagnostically and therapeutically to treat secretory protein processing disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 74

This gene is expressed in the frontal cortex.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, of the motor activity and sensory functions that involve the central nervous system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene

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expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of neural disorders that affect cognitive functions.

FEATURES OF PROTEIN ENCODED BY GENE NO: 75

The translation product of this gene shares sequence homology with inorganic pyrophophatase which is thought to be important in the catalysis the hydrolysis of diphosphate bonds, chiefly in nucleoside di- and triphosphates and essential enzymes that are important for controlling the cellular levels of inorganic pyrophosphate (PPi). The bovine homolog of this gene has been identified by Yang and Wensel (J. Biol. Chem. 267:24641-24647 (1992)).

This gene is expressed in osteoclastoma cells and to a lesser extent in epithelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, osteoporosis and other bone weakening diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., bone, and epithelial cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:199 as residues: Lys-22 to Tyr-28, Asp-64 to Lys-77, Pro-86 to Ile-91, Gln-99 to Pro-119, Tyr-169 to Asp-174, Lys-176 to Gly-181, Trp-189 to Asn-202, Lys-233 to Gly-239, Ser-250 to Asp-257.

The tissue distribution and homology to inorganic pyrophophatase indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of osteoporosis through the removal of bone by demineralization.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 76

The translation product of this gene shares exact sequence homology with ATP sulfurylase/APS kinase (GenBank Accession No. 2673862) which is thought to be important in biosynthesis of the activated sulfate donor, adenosine 3'-phosphate 5'-phosphosulfate, involves the sequential action of two enzyme activities: ATP sulfurylase, which catalyzes the formation of adenosine 5'-phosphosulfate (APS) from ATP and free sulfate, and APS kinase, which subsequently phosphorylates APS to produce adenosine 3'-phosphate 5'-phosphosulfate.

This gene is expressed in osteoclastoma cells and to a lesser extent in developmental tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, antibiotic resistant bacterial infections, osteoarthritis and other auto immune diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune or skeletal structure expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., bone, and developmental tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:200 as residues: Asn-15 to Trp-20, Ser-36 to Gly-41, Pro-103 to Val-110, Pro-134 to Arg-143, Leu-173 to Arg-178, Ser-190 to Ala-197, His-314 to Arg-319, Arg-354 to Asn-362, Asp-391 to Arg-397, Glu-402 to Asp-409, Asp-434 to Leu-439, Glu-441 to Arg-446, Gly-455 to Asp-462, Pro-528 to His-541, Asn-566 to Arg-571, Tyr-574 to Glu-581, Thr-589 to Glu-603.

The tissue distribution and homology to ATP sulfurylase/APS kinase indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment or detection of autoimmune diseases.

FEATURES OF PROTEIN ENCODED BY GENE NO: 77

This polypeptide is identical to the SLP-76-associated protein reported by Musci and colleagues (J. Biol. Chem. 272 (18), 11674-11677 (1997)) and to the FYB protein

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reported by da Silva and coworkers (Proc. Natl. Acad. Sci. U.S.A. (1997) In press). These proteins have been reported to be novel T-cell Proteins which bind FYN and SLP-76 and regulate IL-2 production. Preferred polypeptides encoded by this gene comprise the following amino acid sequence: RITDNPEGKWLGRTARGSYGYIK TTAVEIXYDSLKLKKDSLGAPSRPIEDDQEVYDDVAEQDDISSHSQSGSGGIFPP PPDDDIYDGIEEEDADDGFPAPPKQLDMGDEVYDDVDTSDFPVSSAEMSQGTNV GKAKTEEKDLKKLKKQXKEXKDFRKKFKYDGEIRVLYSTKVTTSITSKKWGT RDLQVKPGESLEVIQTTDDTKVLCRNEEGKYGYVLRSYLADNDGEIYDDIADGC IYDND (SEQ ID NO:322).

This gene is expressed in CD34 positive cells (hematopoietic progenitor cells) and to a lesser extent in adult spleen derived from a chronic lymphocytic leukemia patient.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, chronic lymphocytic leukemia; hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., T-cells and other blood cells, bone marrow, hematopoietic cells, and spleen, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Further, nucleic acids and polypeptides of the present invention are useful both diagnostically and therapeutically in the intervention of immune and other disorders in which the ability to alter IL-2 expression is desired. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:201 as residues: Ala-17 to Lys-37, Val-39 to Ser-45, Lys-59 to His-70, Arg-90 to Leu-95, Lys-97 to Lys-107, Ser-117 to Leu-124, Phe-133 to Ser-138, Trp-146 to Leu-167, Pro-175 to Asn-185, Lys-190 to Ser-211, Pro-213 to Ser-222, His-230 to Pro-235, Pro-240 to Pro-246, Pro-253 to Gly-261, Leu-271 to Leu-303, Leu-305 to Leu-326, Lys-343 to Leu-349, Thr-363 to Leu-371, Arg-373 to Tyr-381, Tyr-391 to Leu-401, Pro-404 to Val-414, Ser-426 to Ser-432, Ile-448 to Ser-457, Gln-462 to Trp-468, Lys-477 to Ser-501, Asp-518 to Ser-523, Ala-541 to Gln-554.

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The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of a variety of hematopoietic disorders. The noted expression of this gene in the hematopoietic progenitor cell compartment - as determined by its expression on CD34 positive hematopoietic stem and progenitor cells - indicates that it plays a critical role in the expansion or proliferation of hematopoietic stem/progenitor cells, as well as in the differentiation of the various blood cell lineages. Thus it could be useful in the reconstitution of the hematopoietic system of patients with leukemias and other hematopoietic diseases.

10 FEATURES OF PROTEIN ENCODED BY GENE NO: 78

This gene is homologous to heparin cofactor II (HCII) which is a 66-kDa plasma glycoprotein that inhibits thrombin rapidly in the presence of dermatan sulfate or heparin.

This gene is expressed in apoptotic and anergic T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, thrombopienia T-cell lymphomas; Hodgkin's lymphoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system - most notably the T-cell compartment, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other blood cells, and lymphoid tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The homology to heparin cofactor II (HCII) and the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic disorders particularly in thrombopoesis, most notably of the T-cell compartment. This could include immune modulation, inflammation, immune surveillance, graft rejection, and autoimmunity.

35 FEATURES OF PROTEIN ENCODED BY GENE NO: 79

The translation product of this gene shares sequence homology with a mouse

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protein believed to represent an integral membrane protein.

This gene is expressed in fetal cochlea and epididymus and to a lesser extent in adult spleen and osteoclastoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, osteoclastoma; disorders of the inner ear; male fertility disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the inner ear; male reproductive tract; bone; and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., cochlea, epididymus and other reproductive tissue, spleen, and bone, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:203 as residues: Lys-13 to Gly-23, Cys-38 to Asp-43, Gly-48 to Trp-53, Cys-223 to Ile-237, Ile-240 to Ser-246.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of hearing and fertility disorders. Likewise, it may have a role in the modulation of immune function and in the treatment of osteoporosis.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 80

The translation product of this gene shares sequence homology with reticulocalbin which is thought to be important in the binding of calcium, particularly within the endoplasmic reticulum.

This gene is expressed in endothelial cells and stromal cells and to a lesser extent in osteoblasts, osteoclasts, and T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, osteoperosis; osteoclastomas; T-cell lymphomas; Hodgkin's disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in

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providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vasculature, bone, and immune systems - particularly the T-cell compartments, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endothelial cells, stromal cells, bone, T-cells and other blood cells, and lymphoid tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:204 as residues: Lys-20 to Arg-27, Pro-32 to Asp-48, Leu-64 to Arg-72, Asp-108 to Lys-114, Glu-128 to Thr-133, Asp-139 to Phe-147, Thr-196 to Ala-204, Tyr-218 to Glu-228, Val-230 to Gln-236, Arg-241 to Lys-255, Glu-276 to Lys-287.

The tissue distribution and homology to reticulocalbin indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of bone disorders such as osteoporosis; the diagnosis and treatment of T-cell lymphomas and Hodgkin's lymphoma; and the treatment of diseases and defects of the vasculature, such as vascular leak syndrome and aberrant angiogenesis that accompanies tumor growth.

FEATURES OF PROTEIN ENCODED BY GENE NO: 81

The translation product of this gene shares sequence homology with a family of peptide transport genes - particularly the AtPTR2-B gene from *Arabidopsis* - which are thought to be important in the uptake of small peptides.

This gene is expressed in a number of fetal tissues, most notably lung, brain, cochlea, and liver/spleen, and to a lesser extent in osteoclastoma and endometrial tumors.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, osteoclastoma; endometrial tumors; cancer; leukemias. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the bone and endometrium, expression of this gene at significantly higher or lower levels may be

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routinely detected in certain tissues (e.g., fetal tissue, pulmonary tissue, bone, brain and other tissue of the nervous system, cochlea, liver, and spleen, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:205 as residues: Lys-186 to Asn-199, Pro-202 to Ala-207.

The tissue distribution and homology to peptide transport genes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the control of cell proliferation, owing to its strong expression in fetal tissues undergoing active cell division, as well as its expression in a variety of tumors or cancers of adult tissues. Potentially, it may regulate the uptake of peptides that stimulate cell proliferation. This gene product may also be useful in stimulating the uptake of a variety of peptide-based drug compounds.

FEATURES OF PROTEIN ENCODED BY GENE NO: 82

This gene is expressed in fetal liver and spleen and to a lesser extent in endothelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, cancer and tumors of a hematopoietic and/or endothelial cell origin; leukemias. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and/or vasculature, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., liver, spleen, endothelial cells, vascular tissue, and tissue and cells of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:206 as residues: Met-1 to Asp-9, Arg-66 to Gly-76, Asp-164 to Arg-171.

The tissue distribution indicates that polynucleotides and polypeptides

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corresponding to this gene are useful for the treatment of disorders of the immune system. Expression of this gene product in both fetal liver/spleen and endothelial cells indicates that it may be expressed in the hemangioblast, the progenitor cell for both the immune system and the vasculature. Thus, it is most likely expressed in hematopoietic stem cells, and may be useful for the expansion of hematopoietic stem and progenitor cells in conjunction with cancer treatment for a variety of leukemias.

FEATURES OF PROTEIN ENCODED BY GENE NO: 84

The translation product of this gene shares sequence homology with NADH dehydrogenase which is thought to be important in cellular metabolism.

This gene is expressed in fetal dura mater and to a lesser extent in T-cells and hypothalamus.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, diseases affecting cellular metabolism. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., fetal tissue, T-cells and other blood cells, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:208 as residues: Pro-27 to Gln-32, Arg-42 to Glu-51.

The tissue distribution and homology to NADH dehydrogenase indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases involving cellular metabolism.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 85

The translation product of this gene shares sequence homology with I-TRAF, a novel TNF receptor associated factor (TRAF)-interacting protein that regulates TNF receptor-mediated signal transduction. This protein is thought to be important in regulating the cellular response to tumor necrosis factor (TNF), which is an important mediator of inflammation.

This gene is expressed in endothelial cells and to a lesser extent in glioblastoma and osteoblastoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, inflammation; glioblastoma and osteoblastoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endothelial cells, bone, and glial cells and tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:209 as residues: Glu-15 to Thr-22, Glu-46 to Leu-62, Arg-103 to Glu-119, Gln-127 to Glu-132, Asn-152 to Trp-158, Gln-191 to Gln-210, Glu-264 to Thr-271, Tyr-282 to Leu-288, Trp-319 to Thr-331, Glu-335 to Ser-348, Ser-353 to Ser-358, Asp-382 to Asn-392.

The tissue distribution and homology to I-TRAF indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of inflammatory diseases, including rheumatoid arthritis, sepsis, inflammatory bowel disease, and psoriasis, particularly where tumor necrosis factor is known to be involved.

FEATURES OF PROTEIN ENCODED BY GENE NO: 86

This gene has homology with a candidate gene involved in X-linked Retinopathy reported by Wong and colleagues (Genomics 15:467-471 (1993)).

This gene is expressed in a T-cell line.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, inflammation and autoimmune diseases; T-cell lymphoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of inflammatory disorders such as sepsis, inflammatory bowel disease, psoriasis, and rheumatoid arthritis as well as autoimmune disease such as lupus. It could also be useful in immune modulation and in the process of immune surveillance. The present invention can be used diagnostically and therapeutically to treat X-linked Retinopathy.

FEATURES OF PROTEIN ENCODED BY GENE NO: 87

This gene is expressed in human brain tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions, which include, but are not limited to, brain disorders; neurodegenerative disorders; tumors of a brain origin. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma,

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urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:211 as residues: Cys-32 to Tyr-38.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of CNS disorders such as epilepsy, paranoia, depression, Alzheimer's disease, and schizophrenia. It could be useful in the survival and/or proliferation of neurons and could effect neuronal regeneration.

| Last AA of ORF | 30 | 44 | 69 | 81 | 38 | 22 | 109 |
|---|---|---|-------------------|-----------------|---|---|---|
| First AA of Secreted Portion | | 27 | 45 | 26 | 25 | 23 | 21 |
| Last AA of Sig Pep | | 26 | 44 | 25 | 24 | 22 | 20 |
| First AA of Sig Pep | | _ | 1 | I | 1 | | |
| AA SEQ ID NO: Y | 125 | 126 | 212 | 213 | 127 | 128 | 129 |
| of AA I First SEQ AA of ID Signal NO: Pep Y | 353 | 128 | 170 | 413 | 66 | 006 | 103 |
| of of Start | 353 | 128 | 170 | 413 | 66 | 006 | 103 |
| 3' NT of Clone Seq. | 1607 | 1786 | 1487 | 1637 | 1212 | 2061 | 733 |
| 5' NT 3' NT 5' NT Of Of Of State Clone Clone NT Seq. Seq. | 247 | 87 | 79 | 394 | | 882 | 10 |
| Total NT Seq. | 1679 | 1830 | 1487 | 1653 | 1212 | 2061 | 1412 |
| SEQ NÖ: NÖ: | | 12 | 86 | 66 | 13 | 4 | 15 |
| Vector | Uni-ZAP XR | Uni-ZAP XR | pBluescript | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | xxxxx 03/19/98 | 209641 02/25/98 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 |
| cDNA Clone ID | HAGEW82 | HAGFY16 | HBMCF37 | HFLQB16 | HALAA60 | HAPBL78 | HASAV70 |
| Gene No. | - | 7 | 2 | 2 | 8 | 4 | S |

| Last AA of ORF | 62 | 29 | 52 | 56 | 215 | 48 |
|--|---|---|---|---|---|---|
| First AA of Secreted Portion | 18 | | 24 | 18 | 19 | 27 |
| Last AA of Sig Pep | 17 | | 23 | 17 | 18 | 26 |
| rirst AA of Sig Pep | 1 | _ | I | 1 | 1 | 1 |
| AA SEQ NO: Y | 130 | 131 | 132 | 133 | 134 | 135 |
| of AA F First SEQ AA of ID Signal NO: Pep Y | 538 | 181 | 98 | 192 | 401 | 793 |
| S' NT of Start Codor | 538 | 181 | 98 | 192 | 401 | 793 |
| 3' NT of Clone Seq. | 088 | 683 | 1007 | 1393 | 1070 | 2011 |
| 5' NT 3' NT of of Clone Clone Seq. Seq. | 276 | - | 98 | 132 | 277 | 614 |
| Total NT Seq. | 1052 | 683 | 1054 | 1393 | 1215 | 2042 |
| SEQ BO: NO: | 16 | 17 | 18 | 19 | 20 | 21 |
| Vector | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 |
| cDNA Clone ID | HBNAF22 | HBNBL77 | HCDDR90 | HCEEF50 | HCEMU42 | HCENE16 |
| Gene No. | 9 | 7 | ∞ | 6 | 10 | = |

| st A f | 7 | | 66 | 08 | 96 | 84 | 9 |
|---|---|---|---|---|--------------------|---|---|
| Last AA of ORF | 67 | 51 | 539 | 8 | 5 | 4 | 200 |
| First AA of Secreted Portion | 24 | 30 | 31 | 23 | 27 | 37 | 28 |
| Last AA of Sig Pep | 23 | 29 | 30 | 22 | 26 | 36 | 27 |
| First AA of Sig Pep | 1 | | - | 1 | | | |
| AA SEQ ID NO: Y | 136 | 137 | 138 | 214 | 139 | 215 | 140 |
| 5' NT of AA First SEQ AA of ID Signal NO: Pep Y | 69 | 68 | 808 | 515 | 196 | 295 | 70 |
| 5' NT of Start Codon | 69 | 68 | 808 | 515 | 196 | 295 | 70 |
| 3' NT of Clone Seq. | 1872 | 289 | 3532 | 1115 | 907 | 734 | 717 |
| 5' NT of Clone Seq. | 21 | - | 2821 | 435 | | 25 | |
| Total NT Seq. | 1872 | 289 | 3533 | 1145 | 1148 | 734 | 717 |
| SEQ NÖ: | 22 | 23 | 24 | 100 | 25 | 101 | 26 |
| Vector | Uni-ZAP XR | ZAP Express | Uni-ZAP XR | Uni-ZAP XR | pBluescript | Uni-ZAP XR | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 209179 07/24/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 |
| cDNA Clone ID | HMSJJ74 | HCUBF15 | HE2DE47 | HE2DE47 | HKMLH01 | HE6DG34 | HE9DG49 |
| Gene No. | 12 | 13 | 41 | 14 | 15 | 15 | 16 |

| Last AA of ORF | 202 | 215 | 185 | 101 | 111 | 19 |
|--|---|---|---|---|---|---|
| First AA of Secreted Portion | 29 | 23 | 26 | 43 | 31 | |
| Last AA of Sig Pep | 28 | 22 | 25 | 42 | 30 | |
| First Last AA AA of of Sig Sig Pep Pep | 1 | 1 | I | 1 | 1 | _ |
| AA SEQ ID NO: Y | 216 | 141 | 217 | 142 | 143 | 144 |
| of AA F First SEQ AA of ID Signal NO: Pep Y | 78 | 38 | 149 | 128 | 294 | 496 |
| of of Start | 78 | 38 | 149 | 128 | 294 | 496 |
| 3' NT of Clone Seq. | 713 | 1099 | 1080 | 941 | 756 | 2093 |
| S' NT 3' NT of of State of Seq. Seq. Cone | 17 | | | 171 | 62 | 408 |
| Total NT Seq. | 713 | 1099 | 1080 | 941 | 756 | 2100 |
| X SEQUENCE OF SEQU | 102 | 27 | 103 | 28 | 29 | 30 |
| Vector | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 |
| cDNA Clone ID | HE9DG49 | HELBA06 | HELBA06 | HSLFM29 | HELBW38 | HETHN28 |
| Gene No. | 16 | 17 | 17 | 18 | 19 | 20 |

| Last AA of ORF | 29 | 86 | 7 | 38 | 130 | 31 | 13 |
|---|---|---|---|---|---|---|-------------------|
| First AA 1 of Secreted Portion (| | . 59 | | 17 | 27 | 22 | |
| Last AA of Sig Pep | | 28 | | 16 | 26 | 21 | |
| First AA of Sig Pep | | | - | 1 | 1 | - | _ |
| SEQ SEQ YÖ: | 145 | 146 | 147 | 148 | 149 | 150 | 151 |
| S' NT of First AA of Signal Pep | 267 | 21 | 210 | 242 | 178 | 144 | 1104 |
| 5' NT of Start Codon | 567 | 21 | 210 | 242 | 178 | 144 | 1104 |
| | 1392 | 409 | 1322 | 710 | 1161 | 938 | 1581 |
| 5' NT 3' NT of of Clone Clone Seq. Seq. | 475 | | - | | 110 | | 974 |
| Total NT Seq. | 1448 | 456 | 1326 | 710 | 1188 | 956 | 1603 |
| SEQ NO: NO: | 31 | 32 | 33 | 34 | 35 | 36 | 37 |
| Vector | Uni-ZAP XR | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97923 03/07/97 209071 05/22/97 | 97924 03/07/97 |
| cDNA Clone ID | HFCDK17 | HFEAF41 | HFKFL13 | HFSBG13 | HFTBE43 | HFTDJ36 | HKTAC77 |
| Gene No. | 21 | 22 | 23 | 24 | 25 | 26 | 27 |

| Last AA of ORF | 7 | 29 | 25 | 194 | 90 | 30 | 68 | 68 | 88 | 173 | 137 | 47 | 44 |
|--|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| First AA of Secreted Portion | | 33 | | 33 | 61 | 31 | 20 | 23 | 19 | 21 | 21 | 28 | 28 |
| Last AA of Sig Pep | | 32 | | 32 | 81 | 30 | 19 | 22 | 18 | 20 | 20 | 27 | 27 |
| First AA of Sig Pep | I | 1 | 1 | T | I | Ţ | 1 | _ | I | I | | I | _ |
| AA SEQ ID NO: Y | 152 | 153 | 154 | 155 | 156 | 157 | 158 | 218 | 159 | 160 | 219 | 220 | 161 |
| 5' NT of First AA of Signal Pep | 607 | 119 | 581 | 126 | 43 | 171 | 5 5 | 58 | 11 | 15 | 72 | 54 | 269 |
| 5' NT of Start Codon | | 119 | 581 | 126 | 43 | 171 | 55 | 58 | 17 | 15 | 72 | 54 | 269 |
| 3' NT of Clone Seq. | 1067 | 629 | 1793 | 1123 | 875 | 843 | 486 | 489 | 534 | 1374 | 640 | 1399 | 596 |
| 5' NT 3' NT of of Clone Clone Seq. | SS | 1 | 408 | 13 | 1 | _ | 3 | 9 | 1 | I | 58 | 40 | 1 |
| Total NT Seq. | 6801 | 679 | 1964 | 1522 | 875 | 843 | 489 | 489 | 534 | 1374 | 640 | 1529 | 596 |
| NT SEQ D NO: X | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 104 | 45 | 46 | 105 | 106 | 47 |
| Vector | pBluescript | pBluescript | Lambda ZAP II | Uni-ZAP XR | Uni-ZAP XR | pSport1 | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97924 03/07/97 |
| cDNA Clone ID | нгнѕнз6 | 96ЛЅНПН | 98ОВОТН | HLTBX31 | HLTCJ63 | HMKAH44 | HMQAJ64 | HMQAJ64 | HOABG65 | HODCL36 | HODCL36 | HODCL36 | HODCL50 |
| Gene No. | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 34 | 35 | 36 | 36 | 36 | 37 |

| Last AA of ORF | 22 | 69 | 775 | 69 | 319 | 82 | 30 | 71 | 280 | 42 | 22 | 326 | 183 |
|---------------------------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| First AA of Secreted Portion | | 81 | 07 | 32 | 61 | 22 | | 19 | 31 | 31 | | 20 | 24 |
| Last AA of Sig Pep | | 17 | 19 | 31 | 09 | 21 | | 18 | 30 | 30 | | 19 | 23 |
| First AA of Sig Pep | 1 | - | | 1 | | 1 | 1 | Ī | | - | | _ | _ |
| AA SEQ ID NO: Y | 162 | 163 | 164 | 221 | 165 | 222 | 991 | 167 | 168 | 223 | 691 | 170 | 224 |
| ال بل ا ال | 170 | 638 | 99 | 928 | 150 | 239 | 432 | 142 | 25 | 433 | 217 | 57 | 35 |
| 5' NT of Start Codon | 170 | 638 | 66 | 928 | 150 | 239 | 432 | 142 | 25 | 433 | 217 | 57 | 35 |
| 3' NT of Clone Seq. | 822 | 2020 | 2432 | 2435 | 2340 | 791 | 601 | 337 | 1141 | 1166 | 1148 | 809 | 586 |
| S' NT 3' NT of Clone Clone Seq. | | | | | 1627 | 62 | 188 | | 1 | 21 | 63 | 164 | 4 |
| Total NT Seq. | 851 | 2020 | 2432 | 2435 | 2340 | 805 | 601 | 359 | 1141 | 1166 | 1560 | 1507 | 286 |
| SEQ NÖ: | 48 | 49 | 50 | 107 | 51 | 108 | 52 | 53 | 54 | 109 | 55 | 26 | 110 |
| Vector | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR | pBluescript SK- | pBluescript SK- | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 | 97924 03/07/97 |
| cDNA Clone ID | HODCV74 | | HTOEU03 | HTOEU03 | HPBCJ74 | HPBCJ74 | HPMBU33 | HSAUL66 | HSIDQ18 | HSIDQ18 | HSJBB37 | HSJBQ79 | HSJBQ79 |
| Gene No. | 38 | 39 | 40 | 40 | 41 | 41 | 42 | 43 | 44 | 44 | 45 | 46 | 46 |

| Last AA of ORF | 89 | 158 | 70 | 122 | 128 | 6 | 371 |
|--|---|---|---|---|---|---|--------------------|
| First AA of Secreted Portion | 36 | 16 | 20 | 19 | 31 | | 2 |
| Last AA of Sig Pep | 35 | 15 | 19 | 18 | 30 | | _ |
| First AA of Sig Pep | | - | I | | | _ | |
| AA SEQ ID NO: Y | 171 | 172 | 225 | 173 | 174 | 226 | 175 |
| 5' NT of First AA of Signal Pep | 83 | 163 | 155 | 115 | 52 | 829 | 114 |
| 5' NT of Start Codon | 83 | 163 | 155 | 115 | 25 | 829 | 114 |
| 3' NT of Clone Seq. | 450 | 1147 | 1134 | 777 | 298 | 1333 | 1554 |
| 5' NT 3' NT of of Clone Clone Seq. Seq. | | 1 | · | | 48 | 594 | 443 |
| Total NT Seq. | 450 | 1147 | 1134 | 777 | 1191 | 1333 | 1580 |
| SEQ NO: NO: | 57 | 58 | 111 | 59 | 09 | 112 | 61 |
| Vector | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR | pBluescript | pBluescript | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 209235 09/04/97 |
| cDNA Clone ID | HTEGA76 | HTEJN13 | HTEJN13 | HTHBL86 | HTSF071 | HTSF071 | HAPNO80 |
| Gene No. | 47 | 48 | 48 | 49 | 50 | 50 | 51 |

| Last AA of ORF | 137 | 215 | 54 | 22 | 102 | 47 |
|--|---|---|---|---|---|---|
| First AA of Secreted Portion | 29 | 29 | 33 | 21 | 34 | 39 |
| | 28 | 28 | 32 | 20 | 33 | 38 |
| First Last AA AA of of Sig Sig Pep Pep | 1 | _ | | 1 | Ţ | 1 |
| AA SEQ ID NO: Y | 227 | 176 | 177 | 178 | 621 | 081 |
| S' NT of AA IF SEQ AA of ID Signal NO: | 244 | 182 | <i>L</i> 6 | 150 | 231 | 703 |
| 5' NT of Start Codon | 244 | 182 | <i>1</i> 6 | 150 | 231 | 703 |
| 3' NT of Clone Seq. | 708 | 1034 | 361 | 1638 | 1303 | 1011 |
| 5' NT 3' NT of of Clone Clone Seq. | 249 | 105 | _ | - | 35 | 655 |
| Total NT Seq. | 1015 | 1117 | 361 | 1668 | 1353 | 1011 |
| SEQ NÖ: NÖ: | 113 | 62 | 63 | 64 | 59 | 99 |
| Vector | Uni-ZAP XR | pBluescript | pSport1 | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 |
| cDNA Clone ID | HAUCC47 | HBMCL41 | HCFLD84 | HE8EM69 | HE8EZ48 | HEBGF73 |
| Gene No. | 51 | 52 | 53 | 54 | 55 | 95 |

| Last AA of ORF | 95 | 94 | 26 | 10 | 64 | 21 |
|--|---|---|---|---|---|---|
| Last AA First AA 1 of of Sig Secreted Pep Portion (| 36 | 30 | 22 | | 20 | 22 |
| Last AA of Sig Pep | 35 | 29 | 21 | | 19 | 21 |
| First AA of of Sig Pep | - | | I | 1 | 1 | Ţ |
| AA SEQ ID NO: Y | 181 | 182 | 183 | 184 | 185 | 186 |
| of AA F of AA F First SEQ AA of ID Signal NO: Pep Y | 459 | 63 | 628 | 270 | 272 | 127 |
| S' NT 3' NT of of of S' NT Figure Clone Clone Of At Start Signal Seq. Seq. Start Signal Seq. | 459 | 63 | 839 | 270 | 272 | 127 |
| 3' NT of Clone Seq. | 1090 | 260 | 1581 | 711 | 935 | 484 |
| 5' NT of Clone Seq. | 267 | - | 765 | ∞ . | 111 | 113 |
| Total NT Seq. | 1193 | 260 | 1657 | 711 | 935 | 504 |
| SEQ NÖ: | <i>L</i> 9 | 89 | 69 | 20 | 71 | 72 |
| Vector | Uni-ZAP XR | Uni-ZAP XR | pBluescript | Lambda ZAP II | Lambda ZAP II | Lambda ZAP II |
| ATCC Deposit Nr and Date | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 |
| cDNA Clone ID | HFEBF41 | HFRBU14 | HFVGZ79 | I . | HHGCO88 | HHGCP52 |
| Gene No. | 57 | 58 | 59 | 09 | 61 | 62 |

| Last AA of ORF | 131 | 89 | 44 | 64 | 22 | 169 |
|--|---|---|---|---|---|---|
| First AA of Secreted Portion | 61 | 33 | 28 | 37 | 12 | 15 |
| | 18 | 32 | 27 | 36 | 11 | 14 |
| AA First Last SEQ AA AA ID of of NO: Sig Sig Y Pep Pep | 1 | | 1 | | _ | 1 |
| AA SEQ ID NO: Y | 187 | 188 | 189 | 190 | 228 | 192 |
| 5' NT of AA 1 First SEQ AA of ID Signal NO: Pep Y | 96 | 248 | 630 | 167 | 575 | 187 |
| of of Start Codon | 96 | 248 | 630 | 167 | | 187 |
| 3' NT of Clone Seq. | 620 | 581 | 1786 | 800 | 1076 | 1888 |
| Son Seq. (Seq. (Se | | 156 | 537 | 116 | 398 | 18 |
| Total NT Seq. | 620 | 581 | 1843 | 1441 | 1076 | 2776 |
| SEQ NÖ: | 73 | 74 | 75 | 76 | 114 | 78 |
| Vector | Lambda ZAP II | Lambda ZAP II | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR | pCMVSport 3.0 |
| ATCC Deposit Nr and Date | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 | 97958 03/13/97 209072 05/22/97 |
| cDNA Clone ID | HHGDB72 | HHGDI71 | HHSDI45 | HHSEB66 | HJPAZ83 | HLDBO49 |
| Gene No. | 63 | 64 | 65 | 99 | 67 | 89 |

| Last AA of ORF | 65 | 131 | 91 | 175 | 69 | 24 | 72 |
|--|---|--------------------|---|---|---|---|---|
| First AA of Secreted Portion | 23 | 23 | 33 | 24 | 27 | 21 | 26 |
| Last AA of Sig Pep | 22 | 22 | 32 | 23 | 26 | 20 | 25 |
| First AA of Sig Pep | 1 | 1 | . 1 | 1 | 1 | 1 | - |
| SEQ NÖ: | 193 | 229 | 194 | 195 | 196 | 161 | 198 |
| 5' NT of First AA of Signal Pep | 534 | 534 | 40 | 238 | 286 | 28 | 14 |
| 5' NT of Start Codon | 534 | 534 | 40 | 238 | 286 | 58 | 14 |
| 3' NT of Clone Seq. | 1480 | 1487 | 1077 | 780 | 770 | 481 | 623 |
| S' NT 3' NT of Clone Clone Seq. | 401 | 401 | 33 | 81 | 101 | | - |
| Total NT Seq. | 1525 | 1487 | 1563 | 1020 | 770 | 481 | 644 |
| NT SEQ BD NO: | 62 | 115 | 08 | 81 | 82 | 83 | 84 |
| Vector | pCMVSport 3.0 | pCMVSport 3.0 | Uni-ZAP XR | Uni-Zap XR | Uni-ZAP XR | Uni-ZAP XR | pCMVSport 3.0 |
| ATCC Deposit Nr and Date | 97958 03/13/97 209072 05/22/97 | 209226 08/28/97 | 97958 03/13/97 209072 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 |
| cDNA Clone ID | нгрв019 | HLDBQ19 | HMSGT42 | HMWIC78 | HTTCT79 | HNGJU84 | HNTAC73 |
| Gene No. | 69 | 69 | 70 | 71 | 72 | 73 | 74 |

| Last AA of ORF | 288 | 27 | 623 | 09 | 648 | 28 |
|--|---|---|---|---|---|---|
| First AA of Secreted Portion | 13 | | 31 | 33 | 31 | 22 |
| | 12 | | 30 | 32 | 30 | 21 |
| First Last AA AA of of Sig Sig Pep Pep | | | Ī | | , - | - |
| AA SEQ ID NO: Y | 199 | 230 | 200 | 231 | 201 | 232 |
| of AA Fi of AA Fi First SEQ AA AA Of ID Signal NO: S | 86 | 545 | 95 | 477 | 251 | 212 |
| | 86 | | 26 | 477 | 251 | 229 |
| 3' NT of Clone Seq. | 1284 | 1283 | 1747 | 1747 | 2566 | 1098 |
| NT SEQ of of S' N SEQ OF St. N Seq. Seq. Cod | 435 | 428 | 290 | 288 | 1843 | 375 |
| Total NT Seq. | 1351 | 1350 | 2527 | 2527 | 2566 | 1098 |
| × Seo | 85 | 116 | 98 | 117 | 87 | 118 |
| Vector | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 |
| cDNA Clone ID | HOSEI45 | HOSEI45 | HOSFD58 | HOSFD58 | HSAUM95 | HSAUM95 |
| Gene No. | 75 | 75 | 92 | 76 | 77 | 77 |

| Last AA of ORF | 54 | 265 | 17 | 314 | 206 | 194 |
|---|---|---|---|---|---|---|
| First AA of Secreted Portion | 33 | 12 | | 20 | 21 | 70 |
| Last AA of Sig Pep | 32 | 11 | | 19 | 20 | 69 |
| AA First Last SEQ AA AA ID of of of NO: Sig Sig Y Pep Pep | _ | I | _ | - | - | |
| AA SEQ DO: Y | 202 | 203 | 233 | 204 | 205 | 206 |
| of AA First SEQ AA of D Signal NO: | 83 | 188 | 315 | 92 | 414 | 157 |
| 5' NT of Start Codon | 83 | 188 | 315 | 92 | 414 | 157 |
| S' NT 3' NT of of Clone Clone Seq. Seq. | 540 | 1165 | 1166 | 2449 | 2058 | 1411 |
| 5' NT 3' NT of of Clone Clone Seq. Seq. | _ | 152 | 152 | 1149 | 476 | 345 |
| Total NT Seq. | 540 | 1863 | 1679 | 2478 | 2058 | 1411 |
| SEQ NÖ: | 88 | 68 | 119 | 06 | 16 | 92 |
| Vector | Uni-ZAP XR | pBluescript |
| ATCC Deposit Nr and Date | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 |
| cDNA Clone ID | HSAUR67 | HSKD181 | HSKD181 | HSKDW91 | HTLEX50 | HSKHL65 |
| Gene No. | 78 | 79 | 79 | 08 | 81 | 82 |

| Last AA of ORF | 71 | 329 | 95 | 57 | 391 | 25 |
|--|---|---|---|---|---|---|
| First AA of Secreted Portion | 38 | 31 | 20 | 21 | 2 | 22 |
| Last AA of Sig Pep | 37 | 30 | 19 | 20 | - | 21 |
| First AA of Sig Pep | 1 | 1 | - | | - | - |
| AA SEQ D NO: Y | 235 | 207 | 236 | 208 | 209 | 210 |
| 5' NT of First AA of Signal Pep | 526 | 397 | 228 | 445 | 523 | 117 |
| of of Start Codon | 526 | 397 | 228 | 445 | 523 | 117 |
| 3' NT of Clone Seq. | 1411 | 2184 | 2063 | 809 | 2394 | 672 |
| 5' NT 3' NT of of Clone Clone Seq. Seq. | 345 | 147 | 138 | 524 | 481 | |
| Total NT Seq. | 1411 | 2187 | 2256 | 757 | 2394 | 672 |
| SEQ NA | 121 | 93 | 122 | 94 | 95 | 96 |
| Vector | pBluescript | Uni-ZAP XR | Uni-ZAP XR | Uni-ZAP XR | ZAP Express | Uni-ZAP XR |
| ATCC Deposit Nr and Date | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 | 97957 03/13/97 209073 05/22/97 |
| cDNA Clone ID | HSKHL65 | HHFGA11 | HHFGA11 | HWTBL40 | HBXFG80 | HCACY32 |
| Gene No. | 82 | 83 | 83 | 84 | 85 | 98 |

| Last AA of ORF | 37 |
|---|---|
| 5' NTAAFirstLastofAAFirstLastT FirstSEQAAAAFirst AALastAA ofIDofofAAt SignalNO:SigSicretedofnnPepYPepPortionORF | 21 |
| Last AA of Sig Pep | 20 |
| First AA of Sig Pep | _ |
| AA SEQ ID NO: Y | 211 |
| 5' NT of First AA of Signal Pep | 207 211 1 20 |
| Song Seq. Seq. Codon | 207 |
| 3' NT of Clone Seq. | 1419 |
| 5' NT of Clone Seq. | - |
| Total NT Seq. | 1419 |
| × Šež Šež | <i>L</i> 6 |
| Vector | Uni-ZAP XR 97 1419 1 1419 207 |
| ATCC Deposit Nr and Date | 97957 03/13/97 209073 05/22/97 |
| cDNA Clone ID | нсер021 |
| Gene No. | 87 |

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Table 1 summarizes the information corresponding to each "Gene No." described above. The nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the "cDNA clone ID" identified in Table 1 and, in some cases, from additional related DNA clones. The overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X.

The cDNA Clone ID was deposited on the date and given the corresponding deposit number listed in "ATCC Deposit No:Z and Date." Some of the deposits contain multiple different clones corresponding to the same gene. "Vector" refers to the type of vector contained in the cDNA Clone ID.

"Total NT Seq." refers to the total number of nucleotides in the contig identified by "Gene No." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5" NT of Clone Seq." and the "3" NT of Clone Seq." of SEQ ID NO:X. The nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5" NT of Start Codon." Similarly, the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5" NT of First AA of Signal Pep."

The translated amino acid sequence, beginning with the methionine, is identified as "AA SEQ ID NO:Y," although other reading frames can also be easily translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

The first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of Sig Pep" and "Last AA of Sig Pep." The predicted first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion." Finally, the amino acid position of SEQ ID NO:Y of the last amino acid in the open reading frame is identified as "Last AA of ORF."

SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to the secreted proteins encoded by the cDNA clones identified in Table 1.

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Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1. The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, or the deposited clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are species homologs. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for the desired homologue.

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below).

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It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural or recombinant sources using antibodies of the invention raised against the secreted protein in methods which are well known in the art.

Signal Sequences

Methods for predicting whether a protein has a signal sequence, as well as the cleavage point for that sequence, are available. For instance, the method of McGeoch, Virus Res. 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, Nucleic Acids Res. 14:4683-4690 (1986) uses the information from the residues surrounding the cleavage site, typically residues -13 to +2, where +1 indicates the amino terminus of the secreted protein. The accuracy of predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, supra.) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.

In the present case, the deduced amino acid sequence of the secreted polypeptide was analyzed by a computer program called SignalP (Henrik Nielsen et al., Protein Engineering 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results shown in Table 1.

As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty. Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO:Y which have an N-terminus beginning within 5 residues (i.e., + or - 5 residues) of the predicted cleavage point. Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely

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uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

10 Polynucleotide and Polypeptide Variants

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

By a polynucleotide having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the polynucleotide is identical to the reference sequence except that the polynucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a polynucleotide having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence shown in Table 1, the ORF (open reading frame), or any fragement specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the presence invention can be determined conventionally using known computer programs. A preferred method for determing the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are:

Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization

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Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is becuase the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignement of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query

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amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequences shown in Table 1 or to the amino acid sequence encoded by deposited DNA clone can be determined conventionally using known computer programs. A preferred method for determing the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or Cterminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and Cterminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the Nterminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini 5 not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-10 termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequnce are manually corrected for. No other manual corrections are to made for the 15 purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as E. coli).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the secreted protein without substantial loss of biological function. The authors of Ron et al., J. Biol. Chem. 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after

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deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

Thus, the invention further includes polypeptide variants which show substantial biological activity. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity. For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie, J. U. et al., Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

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The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

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Polynucleotide and Polypeptide Fragments

In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence contained in the deposited clone or shown in SEQ ID NO:X. The short nucleotide fragments are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in the deposited clone or the nucleotide sequence shown in SEQ ID NO:X. These nucleotide fragments are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments having a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, or 701 to the end of SEQ ID NO:X or the cDNA contained in the deposited clone. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity.

In the present invention, a "polypeptide fragment" refers to a short amino acid sequence contained in SEQ ID NO:Y or encoded by the cDNA contained in the deposited clone. Protein fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, or 161 to the end of the coding region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any

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combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotide fragments encoding these polypeptide fragments are also preferred.

Also preferred are polypeptide and polynucleotide fragments characterized by structural or functional domains, such as fragments that comprise alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet-forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions. Polypeptide fragments of SEQ ID NO:Y falling within conserved domains are specifically contemplated by the present invention. Moreover, polynucleotide fragments encoding these domains are also contemplated.

Other preferred fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Epitopes & Antibodies

In the present invention, "epitopes" refer to polypeptide fragments having antigenic or immunogenic activity in an animal, especially in a human. A preferred embodiment of the present invention relates to a polypeptide fragment comprising an epitope, as well as the polynucleotide encoding this fragment. A region of a protein molecule to which an antibody can bind is defined as an "antigenic epitope." In contrast, an "immunogenic epitope" is defined as a part of a protein that elicits an antibody response. (See, for instance, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983).)

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

In the present invention, antigenic epitopes preferably contain a sequence of at least seven, more preferably at least nine, and most preferably between about 15 to about 30 amino acids. Antigenic epitopes are useful to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe, J. G. et al., Science 219:660-666 (1983).)

Similarly, immunogenic epitopes can be used to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow, M. et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle, F. J. et

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al., J. Gen. Virol. 66:2347-2354 (1985).) A preferred immunogenic epitope includes the secreted protein. The immunogenic epitopes may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if it is long enough (at least about 25 amino acids), without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting.)

As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is meant to include intact molecules as well as antibody fragments (such as, for example, Fab and F(ab')2 fragments) which are capable of specifically binding to protein. Fab and F(ab')2 fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding than an intact antibody. (Wahl et al., J. Nucl. Med. 24:316-325 (1983).) Thus, these fragments are preferred, as well as the products of a FAB or other immunoglobulin expression library. Moreover, antibodies of the present invention include chimeric, single chain, and humanized antibodies.

Fusion Proteins

Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, the polypeptides of the present invention can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

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Moreover, polypeptides of the present invention, including fragments, and specifically epitopes, can be combined with parts of the constant domain of immunoglobulins (IgG), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life in vivo. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP A 394,827; Traunecker et al., Nature 331:84-86 (1988).) Fusion proteins having disulfide-linked dimeric structures (due to the IgG) can also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995).)

Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D. Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).)

Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein. (Wilson et al., Cell 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

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Vectors, Host Cells, and Protein Production

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in E. coli and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as E. coli, Streptomyces and Salmonella typhimurium cells; fungal cells, such as yeast cells; insect cells such as Drosophila S2 and Spodoptera Sf9 cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Other suitable vectors will be readily apparent to the skilled artisan.

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Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., Basic Methods In Molecular Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention, and preferably the secreted form, can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

30 Uses of the Polynucleotides

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat

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polymorphisms), are presently available. Each polynucleotide of the present invention can be used as a chromosome marker.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, and preselection by hybridization to construct chromosome specific-cDNA libraries.

Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes). Preferred polynucleotides correspond to the noncoding regions of the cDNAs because the coding sequences are more likely conserved within gene families, thus increasing the chance of cross hybridization during chromosomal mapping.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library).) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in the polynucleotide and the corresponding gene between affected and unaffected individuals can be examined.

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First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using polynucleotides of the present invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

In addition to the foregoing, a polynucleotide can be used to control gene expression through triple helix formation or antisense DNA or RNA. Both methods rely on binding of the polynucleotide to DNA or RNA. For these techniques, preferred polynucleotides are usually 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques are effective in model systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying

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personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to particular tissue prepared from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination.

In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

Uses of the Polypeptides

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Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

A polypeptide of the present invention can be used to assay protein levels in a biological sample using antibody-based techniques. For example, protein expression in tissues can be studied with classical immunohistological methods. (Jalkanen, M., et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell . Biol. 105:3087-3096 (1987).) Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and technetium (99mTc), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying secreted protein levels in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, 131I, 112In, 99mTc), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously, or intraperitoneally) into the mammal. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of 99mTc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).)

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Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression of a polypeptide of the present invention in cells or body fluid of an individual; (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a disorder.

Moreover, polypeptides of the present invention can be used to treat disease. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B), to inhibit the activity of a polypeptide (e.g., an oncogene), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease. For example, administration of an antibody directed to a polypeptide of the present invention can bind and reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

Biological Activities

The polynucleotides and polypeptides of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides could be used to treat the associated disease.

35 **Immune Activity**

A polypeptide or polynucleotide of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the

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proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, a polynucleotide or polypeptide of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

A polynucleotide or polypeptide of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells. A polypeptide or polynucleotide of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

Moreover, a polypeptide or polynucleotide of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clet formation). For example, by increasing hemostatic or thrombolytic activity, a polynucleotide or polypeptide of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, a polynucleotide or polypeptide of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

A polynucleotide or polypeptide of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

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Examples of autoimmune disorders that can be treated or detected by the present invention include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis, glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitis, and autoimmune inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by a polypeptide or polynucleotide of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

A polynucleotide or polypeptide of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, a polypeptide or polynucleotide of the present invention may also be used to modulate inflammation. For example, the polypeptide or polynucleotide may inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

Hyperproliferative Disorders

A polypeptide or polynucleotide can be used to treat or detect hyperproliferative disorders, including neoplasms. A polypeptide or polynucleotide of the present invention may inhibit the proliferation of the disorder through direct or indirect

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interactions. Alternatively, a polypeptide or polynucleotide of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but are not limited to neoplasms located in the: abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstron's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

Infectious Disease

A polypeptide or polynucleotide of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, the polypeptide or polynucleotide of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of viruses, include, but are not limited to the following DNA and RNA viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes

Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza), Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiollitis, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide of the present invention 15 include, but not limited to, the following Gram-Negative and Gram-positive bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia, Brucellosis, Candidiasis, Campylobacter, 20 Coccidioidomycosis, Cryptococcosis, Dermatocycoses, Enterobacteriaceae (Klebsiella, Salmonella, Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Menigococcal), Pasteurellacea Infections (e.g., Actinobacillus, Heamophilus, Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, 25 and Staphylococcal. These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme 30 Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis, Chlamydia, Syphilis, Diphtheria, Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. A polypeptide or polynucleotide of the present invention can be used to treat or detect 35

any of these symptoms or diseases.

Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following families: Amebiasis, Babesiosis, Coccidiosis,

Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis,

Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas.

These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related),

Malaria, pregnancy complications, and toxoplasmosis. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

Preferably, treatment using a polypeptide or polynucleotide of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

Regeneration

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A polynucleotide or polypeptide of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteocarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vascular (including vascular endothelium), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, a polynucleotide or polypeptide of the present invention may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. A polynucleotide or polypeptide of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue

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regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using a polynucleotide or polypeptide of the present invention to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stoke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotide or polypeptide of the present invention.

15 Chemotaxis

A polynucleotide or polypeptide of the present invention may have chemotaxis activity. A chemotaxic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

A polynucleotide or polypeptide of the present invention may increase chemotaxic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotaxic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that a polynucleotide or polypeptide of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, a polynucleotide or polypeptide of the present invention could be used as an inhibitor of chemotaxis.

Binding Activity

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit

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(antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide, either as a secreted protein or on the cell membrane. Preferred cells include cells from mammals, yeast, Drosophila, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptide from suitably manipulated cells or tissues.

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Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the invention, (b) assaying a biological activity, and (b) determining if a biological activity of the polypeptide has been altered.

Other Activities

A polypeptide or polynucleotide of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide or polynucleotide of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide or polynucleotide of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

A polypeptide or polynucleotide of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, caricadic rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

A polypeptide or polynucleotide of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

Other Preferred Embodiments

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of

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positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Clone Sequence and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Start Codon and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Similarly preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X.

Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which comprises a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the material deposited with the American Type

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Culture Collection and given the ATCC Deposit Number shown in Table 1 for said cDNA Clone Identifier.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the deposit given the ATCC Deposit Number shown in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of the complete open reading frame sequence encoded by said human cDNA clone.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

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A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

The method for identifying the species, tissue or cell type of a biological sample can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

The method for diagnosing a pathological condition can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

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Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1.

Also preferred is a polypeptide, wherein said sequence of contiguous amino acids is included in the amino acid sequence of SEQ ID NO:Y in the range of positions beginning with the residue at about the position of the First Amino Acid of the Secreted Portion and ending with the residue at about the Last Amino Acid of the Open Reading Frame as set forth for SEQ ID NO:Y in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a secreted portion of the secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

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Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method for detecting in a biological sample a polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

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Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

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Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a secreted portion of a human secreted protein comprising an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y beginning with the residue at the position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y wherein Y is an integer set forth in Table 1 and said position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y is defined in Table 1; and an amino acid sequence of a secreted portion of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a secreted protein activity, which method comprises administering to such an individual a pharmaceutical composition comprising an amount of an isolated polypeptide, polynucleotide, or antibody of the claimed invention effective to increase the level of said protein activity in said individual.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

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Examples

Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample

Each cDNA clone in a cited ATCC deposit is contained in a plasmid vector. Table 1 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The table immediately below correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 1 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

| | Vector Used to Construct Library | Corresponding Deposited Plasmid | |
|----|----------------------------------|---------------------------------|--|
| | Lambda Zap | pBluescript (pBS) | |
| | Uni-Zap XR | pBluescript (pBS) | |
| 15 | Zap Express | pBK | |
| | lafmid BA | plafmid BA | |
| | pSport1 | pSport1 | |
| | pCMVSport 2.0 | pCMVSport 2.0 | |
| , | pCMVSport 3.0 | pCMVSport 3.0 | |
| 20 | pCR [®] 2.1 | pCR [®] 2.1 | |

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res.

- 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS.
- The S and K refers to the orientation of the polylinker to the T7 and T3 primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the f1 origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the f1 ori generates sense strand DNA and in the other, antisense.

Vectors pSport1, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain

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DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993).) Vector lafmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR[®]2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 1, as well as the corresponding plasmid vector sequences designated above. 10

The deposited material in the sample assigned the ATCC Deposit Number cited in Table 1 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone identified in Table 1. Typically, each ATCC deposit sample cited in Table 1 comprises a mixture of approximately equal amounts (by weight) of about 50 plasmid DNAs, each containing a different cDNA clone; but such a deposit sample may include plasmids for more or less than 50 cDNA clones, up to about 500 cDNA clones.

Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 1. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to SEQ ID NO:X.

Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized

using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with ³²P-γ-ATP using T4 polynucleotide 25 kinase and purified according to routine methods. (E.g., Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring, NY (1982).) The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. 30 The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate.

These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., Molecular Cloning: A Laboratory

Manual, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 35 1.104), or other techniques known to those of skill in the art.

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Alternatively, two primers of 17-20 nucleotides derived from both ends of the SEQ ID NO:X (i.e., within the region of SEQ ID NO:X bounded by the 5' NT and the 3' NT of the clone defined in Table 1) are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 µl of reaction mixture with 0.5 ug of the above cDNA template. A convenient reaction mixture is 1.5-5 mM MgCl₂, 0.01% (w/v) gelatin, 20 µM each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., Nucleic Acids Res. 21(7):1683-1684 (1993).)

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is

used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

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Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR using primers selected for the cDNA sequence corresponding to SEQ ID NO:X., according to the method described in Example 1. (See also, Sambrook.)

Example 3: Tissue Distribution of Polypeptide

Tissue distribution of mRNA expression of polynucleotides of the present invention is determined using protocols for Northern blot analysis, described by, among others, Sambrook et al. For example, a cDNA probe produced by the method described in Example 1 is labeled with P³² using the rediprimeTM DNA labeling system (Amersham Life Science), according to manufacturer's instructions. After labeling, the probe is purified using CHROMA SPIN-100TM column (Clontech Laboratories, Inc.), according to manufacturer's protocol number PT1200-1. The purified labeled probe is then used to examine various human tissues for mRNA expression.

Multiple Tissue Northern (MTN) blots containing various human tissues (H) or human immune system tissues (IM) (Clontech) are examined with the labeled probe using ExpressHybTM hybridization solution (Clontech) according to manufacturer's protocol number PT1190-1. Following hybridization and washing, the blots are mounted and exposed to film at -70°C overnight, and the films developed according to standard procedures.

Example 4: Chromosomal Mapping of the Polynucleotides

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions: 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on

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either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

5 Example 5: Bacterial Expression of a Polypeptide

A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp^r), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan^r). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.⁶⁰⁰) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high

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affinity and can be purified in a simple one-step procedure (for details see: The OIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM immidazole. Immidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (lacIq). The origin of replication (oriC) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

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Example 6: Purification of a Polypeptide from an Inclusion Body

The following alternative method can be used to purify a polypeptide expressed in *E coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfuidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

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Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A₂₈₀ monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5 µg of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System

In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak Drosophila promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., Virology 170:31-39 (1989).

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Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon and the naturally associated leader sequence identified in Table 1, is amplified using the PCR protocol described in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("Geneclean" BIO 101 Inc., La Jolla, Ca.).

The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

Five μg of a plasmid containing the polynucleotide is co-transfected with 1.0 μg of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA", Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One μg of BaculoGold™ virus DNA and 5 μg of the plasmid are mixed in a sterile well of a microtiter plate containing 50 μl of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10 μl Lipofectin plus 90 μl Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life

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Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 µl of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 μCi of ³⁵Smethionine and 5 µCi 35S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

Example 8: Expression of a Polypeptide in Mammalian Cells

The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from 30 Retroviruses, e.g., RSV, HTLVI, HIVI and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSport 2.0, and pCMVSport 3.0. Mammalian host cells that could be used

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include, human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as dhfr, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No.209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the CMV-enhancer (Boshart et al., Cell 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the vector does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

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The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five µg of the expression plasmid pC6 is cotransfected with 0.5 µg of the plasmid pSVneo using lipofectin (Felgner et al., supra). The plasmid pSV2-neo contains a dominant selectable marker, the neo gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of metothrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 µM, 2 µM, 5 µM, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 -200 µM. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

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Example 9: Protein Fusions

These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the halflife time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion

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proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

GGGATCCGGAGCCCAAATCTTCTGACAAAACTCACACATGCCCACCGTGCC
CAGCACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCCAAAACC
CAAGGACACCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGTGT
GGACGTAAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACG
GCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAAC
AGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTG
AATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAACCCCC
ATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT
GTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCACGGTCAGCCT
GACCTGCCTGGTCAAAGGCTTCTATCCAAGCGACATCGCCGTGGAGTGGGA
GAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCTCCCGTGCTGG
ACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCA
GGTGGCAGCAGGGGAACGTCTTCTCCTCTCTCCGTGTATGCATGAGGCTCTGC
ACAACCACTACACGCAGAAGACCTCTCCCTGTCTCCCGGGTAAATGAGTGC
GACGGCCGCGACTCTTAGAGGAT (SEO ID NO:1)

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Example 10: Production of an Antibody from a Polypeptide

The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) For example, cells expressing a polypeptide of the present invention is administered to an animal to induce the production of sera containing polyclonal antibodies. In a preferred method, a preparation of the secreted protein is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

In the most preferred method, the antibodies of the present invention are monoclonal antibodies (or protein binding fragments thereof). Such monoclonal antibodies can be prepared using hybridoma technology. (Köhler et al., Nature 256:495 (1975); Köhler et al., Eur. J. Immunol. 6:511 (1976); Köhler et al., Eur. J. Immunol. 6:292 (1976); Hammerling et al., in: Monoclonal Antibodies and T-Cell Hybridomas, Elsevier, N.Y., pp. 563-681 (1981).) In general, such procedures involve immunizing an animal (preferably a mouse) with polypeptide or, more preferably, with a secreted polypeptide-expressing cell. Such cells may be cultured in any suitable tissue culture medium; however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 μg/ml of streptomycin.

The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (Gastroenterology 80:225-232 (1981).) The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide.

Alternatively, additional antibodies capable of binding to the polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide.

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Such antibodies comprise anti-idiotypic antibodies to the protein-specific antibody and can be used to immunize an animal to induce formation of further protein-specific antibodies.

It will be appreciated that Fab and F(ab')2 and other fragments of the antibodies of the present invention may be used according to the methods disclosed herein. Such fragments are typically produced by proteolytic cleavage, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')2 fragments). Alternatively, secreted protein-binding fragments can be produced through the application of recombinant DNA technology or through synthetic chemistry.

For in vivo use of antibodies in humans, it may be preferable to use "humanized" chimeric monoclonal antibodies. Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric antibodies are known in the art. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

20 Example 11: Production Of Secreted Protein For High-Throughput Screening Assays

The following protocol produces a supernatant containing a polypeptide to be tested. This supernatant can then be used in the Screening Assays described in Examples 13-20.

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

Plate 293T cells (do not carry cells past P+20) at 2 x 10⁵ cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing a polynucleotide insert, produced by the methods described in Examples 8 or 9, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37°C for 6 hours.

While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with 1x penstrep, or CHO-5 media (116.6 mg/L of CaCl2 (anhyd); 0.00130 mg/L $CuSO_4-5H_2O$; 0.050 mg/L of $Fe(NO_3)_3-9H_2O$; 0.417 mg/L of $FeSO_4-7H_2O$; 311.80 20 mg/L of Kcl; 28.64 mg/L of MgCl₂; 48.84 mg/L of MgSO₄; 6995.50 mg/L of NaCl; 2400.0 mg/L of NaHCO₃; 62.50 mg/L of NaH₂PO₄-H₂0; 71.02 mg/L of Na₂HPO4; .4320 mg/L of ZnSO₄-7H₂O; .002 mg/L of Arachidonic Acid; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic 25 Acid; 0.010 mg/L of Palmitric Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml of L-Asparagine-H₂0; 6.65 mg/ml of L-Aspartic Acid; 29.56 mg/ml of L-Cystine-2HCL-H₂0; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0 30 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL-H₂0; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalainine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tryrosine-2Na-2H₂0; 99.65 mg/ml of L-35 Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of

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Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; and 0.680 mg/L of Vitamin B₁₂; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine; 0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; and 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml appropriate media to each well. Incubate at 37°C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 13-20.

It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide directly (e.g., as a secreted protein) or by the polypeptide inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an activity in a particular assay.

Example 12: Construction of GAS Reporter Construct

One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in

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many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proxial region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:2)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

| | <u>Ligand</u> | tyk2 | <u>JAKs</u> <u>Jak l</u> | Jak2 | Jak3 | <u>STATS</u> | GAS(elements) or ISRE |
|----|---|-----------------------|-----------------------------|-----------------------|-----------------------|--------------------------------|--|
| 5 | IFN family IFN-a/B IFN-g II-10 | + | + + ? | - + ? | - - - | 1,2,3 1 1,3 | ISRE GAS (IRF1>Lys6>IFP) |
| 10 | gp130 family IL-6 (Pleiotrohic) Il-11(Pleiotrohic) OnM(Pleiotrohic) | + ? ? | +++++ | + ? + | ? ? ? | 1,3 1,3 1,3 | GAS (IRF1>Lys6>IFP) |
| 15 | LIF(Pleiotrohic) CNTF(Pleiotrohic) G-CSF(Pleiotrohic) IL-12(Pleiotrohic) | ? -/+ ? + | + + + - | + + ? + | ? ? + | 1,3 1,3 1,3 1,3 | |
| 20 | g-C family IL-2 (lymphocytes) IL-4 (lymph/myeloid) IL-7 (lymphocytes) IL-9 (lymphocytes) IL-13 (lymphocyte) IL-15 | - - - - ? | + + + + + | - - - ? ? | + + + + ? | 1,3,5 6 5 5 6 5 | GAS GAS (IRF1 = IFP >>Ly6)(IgH) GAS GAS GAS GAS |
| 25 | gp140 family IL-3 (myeloid) IL-5 (myeloid) GM-CSF (myeloid) | - - | - - | ++++ | - - - | 5 5 5 | GAS (IRF1>IFP>>Ly6) GAS GAS |
| 30 | Growth hormone fam GH PRL | ? ? | - +/- | ++ | - - | 5 1,3,5 | |
| 35 | EPO Receptor Tyrosine Ki EGF | ? nases ? | -+ | + | - | 5 1,3 | GAS(B-CAS>IRF1=IFP>>Ly6) GAS (IRF1) |
| 40 | PDGF CSF-1 | ? | + | ++ | - | 1,3 1,3 | GAS (not IRF1) |

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To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 13-14, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an Xhol site. The sequence of the 5' primer is: 5':GCGCCTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCGAAATGATTTCCCCGAAATGATTTCCCCGAAATGATTTCCCCGAAATGATTTCCCCGAAATGATTTCCCCGAAATGATTTCCCCCGAAATGATTTCCCCCGAAATGATTTCCCCCGAAATGATTTCCCCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:3)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

5':CTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCGAAATG ATTTCCCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCC CTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGC CCCATGGCTGACTAATTTTTTTTATTTATTTATGCAGAGGCCGAGGCCGCCTCGGC CTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTT TGCAAAAAAGCTT:3' (SEQ ID NO:5)

With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol acetyltransferase (CAT), luciferase, alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

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Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 13-14.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 15 and 16. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, Il-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

Example 13: High-Throughput Screening Assay for T-cell Activity.

The following protocol is used to assess T-cell activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate T-cells. T-cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml genticin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies)

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with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

During the incubation period, count cell concentration, spin down the required number of cells (10⁷ per transfection), and resuspend in OPTI-MEM to a final concentration of 10⁷ cells/ml. Then add 1ml of 1 x 10⁷ cells in OPTI-MEM to T25 flask and incubate at 37°C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Genticin, and 1% Pen-Strep. These cells are treated with supernatants containing a polypeptide as produced by the protocol described in Example 11.

On the day of treatment with the supernatant, the cells should be washed and resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20°C until SEAP assays are performed according to Example 17. The plates containing the remaining treated cells are placed at 4°C and serve as a source of material for repeating the assay on a specific well if desired.

As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

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Example 14: High-Throughput Screening Assay Identifying Myeloid Activity

The following protocol is used to assess myeloid activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate myeloid cells. Myeloid cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 12, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2x10e⁷ U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM Na₂HPO₄.7H₂O, 1 mM MgCl₂, and 675 uM CaCl₂. Incubate at 37°C for 45 min.

Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37°C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

These cells are tested by harvesting $1x10^8$ cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of $5x10^5$ cells/ml. Plate 200 ul cells per well in the 96-well plate (or $1x10^5$ cells/well).

Add 50 ul of the supernatant prepared by the protocol described in Example 11. Incubate at 37°C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 17.

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Example 15: High-Throughput Screening Assay Identifying Neuronal Activity.

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

- 5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:6)
- 5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:7)

Using the GAS:SEAP/Neo vector produced in Example 12, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heatinactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 11. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine

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growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as $5x10^5$ cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to $1x10^5$ cells/well). Add 50 ul supernatant produced by Example 11, 37°C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 17.

Example 16: High-Throughput Screening Assay for T-cell Activity

NF-κB (Nuclear Factor κB) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-κB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF-κB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- κB is retained in the cytoplasm with I- κB (Inhibitor κB). However, upon stimulation, I- κB is phosphorylated and degraded, causing NF- κB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- κB include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-kB promoter element are used to screen the supernatants produced in Example 11. Activators or inhibitors of NF-kB would be useful in treating

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diseases. For example, inhibitors of NF-kB could be used to treat those diseases related to the acute or chronic activation of NF-kB, such as rheumatoid arthritis.

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene) Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGACTTTCC ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCA TCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACT AATTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTC CAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTT: 3' (SEQ ID NO:10)

Next, replace the SV40 minimal promoter element present in the pSEAP2-promoter plasmid (Clontech) with this NF-κB/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF-κB/SV40/SEAP cassette is removed from the above NF-κB/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the NF-κB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

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Once NF-κB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 13. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described in Example 13. As a positive control, exogenous TNF alpha (0.1,1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

Example 17: Assay for SEAP Activity

As a reporter molecule for the assays described in Examples 13-16, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 μ l of 2.5x dilution buffer into Optiplates containing 35 μ l of a supernatant. Seal the plates with a plastic sealer and incubate at 65°C for 30 min. Separate the Optiplates to avoid uneven heating.

Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 µl Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 µl Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

Reaction Buffer Formulation:

| Reaction 1 | outier Politiciation. | |
|-------------|-------------------------|-----------|
| # of plates | Rxn buffer diluent (ml) | CSPD (ml) |
| 10 | 60 | 3 |
| 11 | 65 | 3.25 |
| 12 | 70 | 3.5 |
| 13 | 75 | 3.75 |
| 14 | 80 | 4 |
| 15 | 85 | 4.25 |
| 16 | 90 | 4.5 |
| 17 | 95 | 4.75 |
| 18 | 100 | 5 |
| 19 | 105 | 5.25 |
| 20 | 110 | 5.5 |
| 21 | 115 | 5.75 |
| 22 | 120 | 6 |

| 23 | 125 | 6.25 |
|------|-----|-------|
| 24 | 130 | 6.5 |
| 25 | 135 | 6.75 |
| 26 | 140 | 7 |
| · 27 | 145 | 7.25 |
| 28 | 150 | 7.5 |
| 29 | 155 | 7.75 |
| 30 | 160 | 8 |
| 31 | 165 | 8.25 |
| 32 | 170 | 8.5 |
| 33 | 175 | 8.75 |
| 34 | 180 | 9 |
| 35 | 185 | 9.25 |
| 36 | 190 | 9.5 |
| 37 | 195 | 9.75 |
| 38 | 200 | 10 |
| 39 | 205 | 10.25 |
| 40 | 210 | 10.5 |
| 41 | 215 | 10.75 |
| 42 | 220 | 11 |
| 43 | 225 | 11.25 |
| 44 | 230 | 11.5 |
| 45 | 235 | 11.75 |
| 46 | 240 | 12 |
| 47 | 245 | 12.25 |
| 48 | 250 | 12.5 |
| 49 | 255 | 12.75 |
| 50 | 260 | 13 |

Example 18: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-3, used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO₂ incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

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A stock solution of 1 mg/ml fluo-3 is made in 10% pluronic acid DMSO. To load the cells with fluo-3, 50 ul of 12 ug/ml fluo-3 is added to each well. The plate is incubated at 37° C in a CO_2 incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10⁶ cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-3 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37°C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10⁶ cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley CellWash with 200 ul, followed by an aspiration step to 100 ul final volume.

For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-3. The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event which has resulted in an increase in the intracellular Ca⁺⁺ concentration.

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Example 19: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

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Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

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Because of the wide range of known factors capable of stimulating tyrosine kinase activity, the identification of novel human secreted proteins capable of activating tyrosine kinase signal transduction pathways are of interest. Therefore, the following protocol is designed to identify those novel human secreted proteins capable of activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford,MA), or calf serum, rinsed with PBS and stored at 4°C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford,MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 11, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na3VO4, 2 mM Na4P2O7 and a cocktail of protease inhibitors (# 1836170) obtained from Boeheringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4°C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a

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biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg₂₊ (5mM ATP/50mM MgCl₂), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl₂, 5 mM MnCl₂, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30°C for 2 min. Initial the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mm EDTA and place the reactions on ice.

Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37°C for 20 min. This allows the streptavadin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phospotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37°C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of tyrosine kinase activity.

Example 20: High-Throughput Screening Assay Identifying Phosphorylation Activity

As a potential alternative and/or compliment to the assay of protein tyrosine kinase activity described in Example 19, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other

phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (lug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4°C until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 11 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (lug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation.

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Example 21: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky, D., et al., Science 252:706 (1991).

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PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies).

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The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

PCR products is cloned into T-tailed vectors as described in Holton, T.A. and Graham, M.W., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenindeoxy-uridine 5'-triphosphate (Boehringer Manheim), and FISH performed as described in Johnson, Cg. et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson, Cv. et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

Example 22: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10.

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The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

Example 23: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1 µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1 µg/kg/hour to about 50 µg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracistemally, intravaginally,

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intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semi-permeable polymer matrices in the form of shaped articles, e.g., films, or mirocapsules. Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., Biopolymers 22:547-556 (1983)), poly (2-hydroxyethyl methacrylate) (R. Langer et al., J. Biomed. Mater. Res. 15:167-277 (1981), and R. Langer, Chem. Tech. 12:98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE 3,218,121; Epstein et al., Proc. Natl. Acad. Sci. USA 82:3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides.

Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

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The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

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Example 24: Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 23.

Example 25: Method of Treating Increased Levels of the Polypeptide

Antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 23.

Example 26: Method of Treatment Using Gene Therapy

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

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At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

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It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference.

```
(1) GENERAL INFORMATION:
                            Human Genome Sciences, Inc. et al.
           (i) APPLICANT:
           (ii) TITLE OF INVENTION: 87 Human Secreted Proteins
           (iii) NUMBER OF SEQUENCES: 323
5
           (iv) CORRESPONDENCE ADDRESS:
                 (A) ADDRESSEE: Human Genome Sciences, Inc.
                 (B) STREET: 9410 Key West Avenue
10
                 (C) CITY: Rockville
                 (D) STATE: Maryland
                 (E) COUNTRY: USA
                  (F) ZIP: 20850
15
           (v) COMPUTER READABLE FORM:
                  (A) MEDIUM TYPE: Diskette, 3.50 inch, 1.4Mb storage
                  (B) COMPUTER: HP Vectra 486/33
20
                  (C) OPERATING SYSTEM: MSDOS version 6.2
                  (D) SOFTWARE: ASCII Text
           (vi) CURRENT APPLICATION DATA:
25
                  (A) APPLICATION NUMBER:
                  (B) FILING DATE: March 19, 1998
                  (C) CLASSIFICATION:
30
           (vii) PRIOR APPLICATION DATA:
                  (A) APPLICATION NUMBER:
                  (B) FILING DATE:
            (viii) ATTORNEY/AGENT INFORMATION:
35
                  (A) NAME: A. Anders Brookes
                  (B) REGISTRATION NUMBER: 36,373
                  (C) REFERENCE/DOCKET NUMBER: PZ004PCT
40
            (vi) TELECOMMUNICATION INFORMATION:
                  (A) TELEPHONE: (301) 309-8504
                  (B) TELEFAX: (301) 309-8439
45
      (2) INFORMATION FOR SEQ ID NO: 1:
            (i) SEQUENCE CHARACTERISTICS:
                  (A) LENGTH: 733 base pairs
50
                  (B) TYPE: nucleic acid
                  (C) STRANDEDNESS: double
                  (D) TOPOLOGY: linear
            (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:
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| | GGGATCCGGA GCCCAAATCT TCTGACAAAA CTCACACATG CCCACCGTGC CCAGCACCTG | 60 |
|----------|--|-----|
| | ANTTCGAGGG TGCACCGTCA GTCTTCCTCT TCCCCCCAAA ACCCAAGGAC ACCCTCATGA | 120 |
| 5 | . TCTCCCGGAC TCCTGAGGTC ACATGCGTGG TGGTGGACGT AAGCCACGAA GACCCTGAGG | 180 |
| | TCAAGTTCAA CTGGTACGTG GACGGCGTGG AGGTGCATAA TGCCAAGACA AAGCCGCGGG | 240 |
| 10 | AGGAGCAGTA CAACAGCACG TACCGTGTGG TCAGCGTCCT CACCGTCCTG CACCAGGACT | 300 |
| 10 | GGCTGAATGG CAAGGAGTAC AAGTGCAAGG TCTCCAACAA AGCCCTCCCA ACCCCCATCG | 360 |
| | AGAAAACCAT CTCCAAAGCC AAAGGGCAGC CCCGAGAACC ACAGGTGTAC ACCCTGCCCC | 420 |
| 15 | CATCCCGGGA TGAGCTGACC AAGAACCAGG TCAGCCTGAC CTGCCTGGTC AAAGGCTTCT | 480 |
| | ATCCAAGCGA CATCGCCGTG GAGTGGGAGA GCAATGGGCA GCCGGAGAAC AACTACAAGA | 540 |
| 10 | CCACGCCTCC CGTGCTGGAC TCCGACGGCT CCTTCTTCCT CTACAGCAAG CTCACCGTGG | 600 |
| 20 | ACAAGAGCAG GTGGCAGCAG GGGAACGTCT TCTCATGCTC CGTGATGCAT GAGGCTCTGC | 660 |
| | ACAACCACTA CACGCAGAAG AGCCTCTCCC TGTCTCCGGG TAAATGAGTG CGACGGCCGC | 720 |
| 25 | GACTCTAGAG GAT | 733 |
| 30 35 | (2) INFORMATION FOR SEQ ID NO: 2: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 5 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2: | |
| 40 | Trp Ser Xaa Trp Ser 1 5 | |
| 45 | (2) INFORMATION FOR SEQ ID NO: 3: | |
| 50 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 86 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3: | |
| 55 | GCGCCTCGAG ATTTCCCCGA AATCTAGATT TCCCCGAAAT GATTTCCCCG AAATGATTTC | 6 |

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CCCGAAATAT CTGCCATCTC AATTAG

| | (2) INFORMATION FOR SEQ ID NO: 4: | |
|----|--|-----|
| 5 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 27 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 10 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4: | |
| | GCGGCAAGCT TTTTGCAAAG CCTAGGC | 27 |
| 15 | | |
| | (2) INFORMATION FOR SEQ ID NO: 5: | |
| 20 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 271 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| 25 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5: | |
| | CTCGAGATTT CCCCGAAATC TAGATTTCCC CGAAATGATT TCCCCGAAAT GATTTCCCCG | 60 |
| 20 | AAATATCTGC CATCTCAATT AGTCAGCAAC CATAGTCCCG CCCCTAACTC CGCCCATCCC | 120 |
| 30 | GCCCCTAACT CCGCCCAGTT CCGCCCATTC TCCGCCCCAT GGCTGACTAA TTTTTTTTAT | 180 |
| | TTATGCAGAG GCCGAGGCCG CCTCGGCCTC TGAGCTATTC CAGAAGTAGT GAGGAGGCTT | 240 |
| 35 | TTTTGGAGGC CTAGGCTTTT GCAAAAAGCT T | 271 |
| 40 | (2) INFORMATION FOR SEQ ID NO: 6: | |
| 45 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6: | |
| 50 | GCGCTCGAGG GATGACAGCG ATAGAACCCC GG | 32 |
| 55 | (2) INFORMATION FOR SEQ ID NO: 7: | |
| | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 31 base pairs(B) TYPE: nucleic acid | |
| 60 | (C) STRANDEDNESS: double | |

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| | (D) TOPOLOGY: linear | |
|----|--|-----|
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7: | |
| 5 | GCGAAGCTTC GCGACTCCCC GGATCCGCCT C | 31 |
| 10 | (2) INFORMATION FOR SEQ ID NO: 8: | |
| 15 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 12 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 20 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8: | |
| 20 | GGGGACTTTC CC | 12 |
| | | |
| 25 | (2) INFORMATION FOR SEQ ID NO: 9: | |
| 30 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 73 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 35 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9: | |
| | GCGGCCTCGA GGGGACTTTC CCGGGGACTT TCCGGGGACT TTCCATCCTG | 60 |
| 40 | CCATCTCAAT TAG | 73 |
| | (a) | |
| 45 | (2) INFORMATION FOR SEQ ID NO: 10: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 256 base pairs | |
| 50 | (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 50 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10: | |
| | CTCGAGGGGA CTTTCCGGG GACTTTCCGG GGACTTTCCA TCTGCCATCT | 60 |
| 55 | CAATTAGTCA GCAACCATAG TCCCGCCCCT AACTCCGCCC ATCCCGCCCC TAACTCCGCC | 120 |
| | CAGTTCCGCC CATTCTCCGC CCCATGGCTG ACTAATTTTT TTTATTTATG CAGAGGCCGA | 180 |
| | GGCCGCCTCG GCCTCTGAGC TATTCCAGAA GTAGTGAGGA GGCTTTTTTG GAGGCCTAGG | 240 |

| CTTTTGCAAA AAGCTT | 256 |
|-------------------|-----|
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(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1679 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

15 GCAGCGCACC CGGGCGATCG CTTCACGGAT GCGGACGACG TAGCCATCCT TACCTACGTG 60 AAGGAAAATG CCCGCTCGCC CAGCTCCGTC ACCGGTAACG CCTTGTGGAA AGCGATGGAG 120 AAGAGCTCGC TCACGCAGCA CTCGTGGCAG TCCCTGAAGG ACCGCTACCT CAAGCACCTG 20 180 CGGGGCCAGG AGCATAAGTA CCTGCTGGGG GACGCGCCGG TGAGCCCCTC CTCCCAGAAG 240 300 CTCAAGCGGA AGGCGGAGGA GGACCCGGAG GCCGCGGATA GCGGGGAACC ACAGAATAAG 25 AGAACTCCAG ATTTGCCTGA AGAAGAGTAT GTGAAGGAAG AAATCCAGGA GAATGAAGAA 360 GCAGTCAAAA AGATGCTTGT GGAAGCCACC CGGGAGTTTG AGGAGGTTGT GGTGGATGAG 420 AGCCCTCCTG ATTTTGAAAT ACATATAACT ATGTGTGATG ATGATCCACC CACACCTGAG 480 30 GAAGACTCAG AAACACAGCC TGATGAGGAG GAAGAAGAAG AAGAAGAAAA AGTTTCTCAA 540 CCAGAGGTGG GAGCTGCCAT TAAGATCATT CGGCAGTTAA TGGAGAAGTT TAACTTGGAT 600 35 CTATCAACAG TTACACAGGC CTTCCTAAAA AATAGTGGTG AGCTGGAGGC TACTTCCGCC 660 TTCTTAGCGT CTGGTCAGAG AGCTGATGGA TATCCCATTT GGTCCCGACA AGATGACATA 720 GATTTGCAAA AAGATGATGA GGATACCAGA GAGGCATTGG TCAAAAAATT TGGTGCTCAG 780 40 840 AAAGTCATGG TAGGTGAGGT GGTTAAAAAA AATTGTGACC AATGAACTTT AGAGAGTTCT 900 45 TGCATTGGAA CTGGCACTTA TTTTCTGACC ATCGCTGCTG TTGCTCTGTG AGTCCTAGAT 960 TTTTGTAGCC AAGCAGAGTT GTAGAGGGGG ATAAAAAGAA AAGAAATTGG ATGTATTTAC 1020 AGCTGTCCTT GAACAAGTAT CAATGTGTTT ATGAAAGGAA GATCTAAATC AGACAGGAGT 1080 50 TGGTCTACAT AGTAGTAATC CATTGTTGGA ATGGAACCCT TGCTATAGTA GTGACAAAGT 1140 GAAAGGAAAT TTAGGAGGCA TAGGCCATTT CAGGCAGCAT AAGTAATCTC CTGTCCTTTG 1200 55 GCAGAAGCTC CTTTAGATTG GGATAGATTC CAAATAAAGA ATCTAGAAAT AGGAGAAGAT 1260 TTAATTATGA GGCCTTGAAC ACGGATTATC CCCAAACCCT TGTCATTTCC CCCAGTGAGC 1320 1380 60 TCTGATTTCT AGACTGCTTT GAAAATGCTG TATTCATTTT GCTAACTTAG TATTTGGGTA

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| | CCCTGCTCTT | TGGCTGTTCT | TTTTTTGGAG | CCCTTCTCAG | TCAAGTCTGC | CGGATGTCTT | 1440 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | TCTTTACCTA | CCCCTCAGTT | TTCCTTAAAA | CGCGCACACA | ACTCTAGAGA | GTGTTAAGAA | 1500 |
| 3 | TAATGTTACT | TGGTTAATGT | GTTATTTATT | GAGTATTGTT | TGTGCTAAGC | ATTGTGTTAG | 1560 |
| | ATTTAAAAAA | TTAGTGGATT | GACTCCACTT | TGTTGTGTTG | TTTTCATTGT | TGAAAATAAA | 1620 |
| 10 | TATAACTTTG | TATTCGAAAA | АААААААА | AAAATNRCTG | CGGNCCGACA | AGGGAATTC | 1679 |

15 (2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1830 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

| 25 | GCGACCGCGC | CCTTCAGCTA | GCTCGCTCGC | TCGCTCTGCT | TCCCTGCTGC | CGGCTGCGCA | 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| | TGGCTTNGGC | GTTGGCGGCG | CTGGCGGCGG | TCGAGCNGCC | TGCGSAGCCG | GTACCAGCAG | 120 |
| 30 | TTGCAGAATG | AAGAAGAGTC | TGGAGAACCT | GAACAGGCTG | CAGGTGATGC | TCCTCCACCT | 180 |
| 50 | TACAGCAGCA | TTTCTGCAGA | GAGCGCACAT | NATTTTGACT | ACAAGGATGA | GTCTGGGTTT | 240 |
| | CCAAAGCCCC | CATCTTACAA | TGTAGCTACA | ACACTGCCCA | GTTATGATGA | AGCGGAGAGG | 300 |
| 35 | ACCAAGGCTG | AAGCTACTAT | CCCTTTGGTT | CCTGGGAGAG | ATGAGGATTT | TGTGGGTCGG | 360 |
| | GATGATTTTG | ATGATGCTGA | CCAGCTGAGG | ATAGGAAATG | ATGGGATTTT | CATGTTAACT | 420 |
| 40 | TTTTTCATGG | CATTCCTCTT | TAACTGGATT | GGGTTTTTCC | TGTCTTTTTG | CCTGACCACT | 480 |
| | TCAGCTGCAG | GAAGGTATGG | GGCCATTTCA | GGATTTGGTC | TCTCTCTAAT | TAAATGGATC | 540 |
| | CTGATTGTCA | GGTTTTCCAC | CTATTTCCCT | GGATATTTTG | ATGGTCAGTA | CTGGCTCTGG | 600 |
| 45 | TGGGTGTTCC | TTGTTTTAGG | CTTTCTCCTG | TTTCTCAGAG | GATTTATCAA | TTATGCAAAA | 660 |
| | GTTCGGAAGA | TGCCAGAAAC | TTTCTCAAAT | CTCCCCAGGA | CCAGAGTTCT | CTTTATTTAT | 720 |
| 50 | TAAAGATGTT | TTCTGGCAAA | GGCCTTCCTG | CATTTATGAA | TTCTCTCTCA | AGAAGCAAGA | 780 |
| 50 | GAACACCTGC | AGGAAGTGAA | TCAAGATGCA | GAACACAGAG | GAATAATCAC | CTGCTTTAAA | 840 |
| | AAAATAAAGT | ACTGTTGAAA | AGATCATTTC | TCTCTATTTG | TTCCTAGGTG | TAAAATTTTA | 900 |
| 55 | ATAGTTAATG | CAGAATTCTG | TAATCATTGA | ATCATTAGTG | GTTAATGTTT | GAAAAAGCTC | 960 |
| | TTGCAATCAA | GTCTGTGATG | TATTAATAAT | GCCTTATATA | TTGTTTGTAG | TCATTTTAAG | 1020 |
| 60 | TAGCATGAGC | CATGTCCCTG | TAGTCGGTAG | GGGGCAGTCT | TGCTTTATTC | ATCCTCCATC | 1080 |

| | TCAAAATGAA | CTTGGAATTA | AATATTGTAA | GATATGTATA | ATGCTGGCCA | TTTTAAAGGG | 1140 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GTTTTCTCAA | AAGTTAAACT | TTTGTTATGA | CTGTGTTTTT | GCACATAATC | CATATTTGCT | 1200 |
| 5 | GTTCAAGTTA | ATCTAGAAAT | TTATTCAATT | CTGTATGAAC | ACCTGGAAGC | AAAATCATAG | 1260 |
| | TGCAAAAATA | CATTTAAGGT | GTGGTCAAAA | ATAAGTCTTT | AATTGGTAAA | TAATAAGCAT | 1320 |
| 10 | TAATTTTTA | TAGCCTGTAT | TCACAATTCT | GCGGTACCTT | ATTGTACCTA | AGGGATTCTA | 1380 |
| 10 | AAGGTGTTGT | CACTGTATAA | AACAGAAAGC | ACTAGGATAC | AAATGAAGCT | TAATTACTAA | 1440 |
| | AATGTAATTC | TTGACACTCT | TTCTATAATT | AGCGTTCTTC | ACCCCCACCC | CCACCCCAC | 1500 |
| 15 | CCCCCTTATT | TTCCTTTTGT | CTCCTGGTGA | TTAGGCCAAA | GTCTGGGAGT | AAGGAGAGGA | 1560 |
| | TTAGGTACTT | AGGAGCAAAG | AAAGAAGTAG | CTTGGAACTT | TTGAGATGAT | CCCTAACATA | 1620 |
| 20 | CTGTACTACT | TGCTTTTACA | ATGTGTTAGC | AGAAACCAGT | GGGTTATAAT | GTAGAATGAT | 1680 |
| 20 | GTGCTTTCTG | CCCAAGTGGT | AATTCATCTT | GGTTTGCTAT | GTTAAAACTG | TAAATACAAC | 174 |
| | AGAACATTAA | TAAATATCTC | TTGTGTAGCA | CCTTTTAAAA | АААААААА | AAAAAAAA | 180 |
| 25 | ааааааааа | AANCCCGGGG | GGGGCCCCN | | | | 183 |

30 (2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1212 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

| 40 | TGTTTGAAGT | TGTTACTTTT | GTTTACAGCA | AAGTTTGATG | TAGTGTGCAG | TAGTGAGCTC | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| | TAGACTGATC | TTTTTCTAAA | TCAGAAAGTG | ATTAAAGTAT | GCACAACCAA | AGGCAGGTTT | 120 |
| 45 | TTCTTTTTCA | TTTATTCAGC | AACTATTTAT | TAAGCATCAA | CTCTGTGCCA | GGCACGTTAC | 180 |
| 45 | TAGCTGCTAC | ATACTGTCTG | AACATGACAT | ACGGTTAAGT | AACTTTACAA | TTATTATCAA | 240 |
| | ATACTTCAAT | GTAGATATTT | CTTAAGTTGA | AATAGCATTA | ACTAGGATAA | TGCTTTCATG | 300 |
| 50 | TTATTTTATT | TGTCTTGTGA | TAGAAATTCA | ACTTTGTACC | ATCTTAAAAC | TAGGTTGCTA | 360 |
| | TAAAAATAGG | AGGATGAAGT | CAATAAAGTT | TATGCCAGTT | TAAAAACTGG | AAGGAAAAGG | 420 |
| 55 | TAAGAGCTCT | CCATTATAAA | ATAGTTGCAT | TCGGTTAATT | TTTACACATT | AGTGCATTGC | 480 |
| | GTATATCAAC | TGGCCCTCAA | TGAAGCATTT | AAGTGCTTGG | AATTTTACTA | AACTGACTTT | 540 |
| | TTTGCAACTT | TGGGAGATTT | TTGAGGGGAG | TGTTGAAAAT | TGCCAAACAC | TCACCTCTTA | 600 |
| 60 | CTCAAAACTT | САААТААААТ | ACACATTTTC | AAGAGGGAGC | ACCTITTATA | TTTGATAAGT | 660 |

| | TTTCATTATA | AACCTTATAA | TACCAGTCAC | AAAGAGGTTG | TCTGTCTATG | GTTTAGCAAA | 720 |
|-----|------------|------------|------------|------------|------------|------------|------|
| 5 | CATTTGCTTT | TCTTTTTGGA | AGTGTGATTG | CAATTGCAGA | ACAGAAAGTG | AGAAAACACT | 780 |
| 3 | GCCAGCGGTG | ATTGCTACTT | GAGGTAGTTT | TTTACAACTA | CCATTTCCCC | TCCATGAAAT | 840 |
| | TATGTGAAAT | TTATTTTATC | TTTGGGAAAA | GTTGAGAAGA | TAGTAAAAGA | ATTAGGAATT | 900 |
| 10 | TAAAATTACA | GGGAAAAATA | TGTAAGTGAA | AAGCAATAAA | TATTTTGTTC | ACTTTGCTAT | 960 |
| | CAAGATGTTC | ACTATCAGAT | ATTTATTATA | TGGCAGCAAT | TTATATTTT | AATCATTGCC | 1020 |
| 1.5 | CATTAATAGA | CGCAGTAAAA | TATTTTTGAA | TCAGACATTT | GGGGTTTGTA | TGTGCATTAA | 1080 |
| 15 | AATTGTCTTT | TGTACTGTAA | GTTACTGTTA | ATTTGAATAT | TTTATTGAAC | TGTCTCCCTG | 1140 |
| | TGCCTTTATA | ATATAAAGTT | GTTTCTACAA | CTTTTAATGA | TCTTAATAAA | GAATACTTTA | 1200 |
| 20 | AGAAAAAAAA | AA | | | | | 1212 |
| | | | | | | | |
| | | | | | | | |

25 (2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2061 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

| 35 | GGTTTTCCTC | CGACTTCCGG | ACATCTCCCT | GGGAGTCGCG | CAGAGTGGAG | TCAAAGGCAA | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| | CCAGTGCTCG | CTGCGGTCTC | TGGGGATCGG | GACCGCGGCG | GCGGCCCGCG | AGCGGGATGT | 120 |
| 40 | TCCGGGGCTT | GAGCAGTTGG | TTGGGCTTGC | AGCAGCCGGT | GGCAGGCGGT | GGGCAGCCCA | 180 |
| 40 | ATGGAGATGC | TCCACCCGAG | CAGCCGTCCG | AGACGGTGGC | TGAGTCTGCG | GAGGAGGAGC | 240 |
| | TGCAGCAAGC | GGGAGACCAG | GAGCTCCTCC | ACCAGGCCAA | AGACTTCGGC | AACTATTTAT | 300 |
| 45 | TTAACTTTGC | ATCTGCTGCC | ACAAAAAAGA | TAACTGAATC | AGTTGCTGAA | ACAGCACAAA | 360 |
| | CAATAAAGAA | ATCCGTAGAA | GAAGGAAAAA | TAGATGGCAT | CATTGACAAG | ACAATTATAG | 420 |
| 50 | GAGATTTTCA | GAAGGAACAG | AAAAAATTTG | TTGAAGAGCA | ACATACAAAG | AAGTCAGAAG | 480 |
| 50 | CAGCTGTGCC | CCCATGGGTT | GACACTAACG | ATGAAGAAAC | AATTCAACAA | CAAATTTTGG | 540 |
| | CCTTATCAGC | TGACAAGAGG | AATTTCCTTC | GTGACCCTCC | GGCTGGCGTG | CAATTTAATT | 600 |
| 55 | TCGACTTTGA | TCAGATGTAC | CCCGTGGCCC | TGGTCATGCT | CCAGGAGGAT | GAGCTGCTAR | 660 |
| | CAAGATGAGA | TTTGCCCTCG | TTCCTAAACT | TGTGAAGGAA | GAAGTGTTCT | GGAGGAACTA | 720 |
| 60 | CTTTTACCGC | GTCTCCCTGA | TTAAGCAGTC | AGCCCAGCTC | ACGGCCCTGG | CTGCCCAACA | 780 |

| | GCAGGCCGCA | GGGAAGGGAG | GAGAAGAGCA | ATGGCAGAGA | GCAAGATTTG | CCGCTGGAGA | 840 |
|-----|------------|---------------------|-----------------------------|--------------|------------|------------|------|
| | GGCAGTACGG | CCCAAAACGC | CACCCGTTGT | AATCAAATCT | CAGCTTAAAA | CTCAAGAGGA | 900 |
| 5 | TGAGGAAGAA | ATTTCTACTA | GCCCAGGTGT. | TTCTGAGTTT | GTCAGTGATG | CCTTCGATGC | 960 |
| | CTGTAACCTA | AATCAGGAAG | ATCTAAGGAA | AGAAATGGAG | CAACTAGTGC | TTGACAAAAA | 1020 |
| 10 | GCAAGAGGAG | ACAGCCGTAC | TGGAAGAGGA | TTCTGCAGAT | TGGGAAAAAG | AACTGCAGCA | 1080 |
| i U | GGAACTTCAA | GAATATGAAG | TGGTGACAGA | ATCTGAAAAA | CGAGATGAAA | ACTGGGATAA | 1140 |
| | GGAAATAGAG | AAAATGCTTC | AAGAGGAAAA | TTAGCTGTTC | CTGAAATAGA | AGAATAATCC | 1200 |
| 15 | TTAACAGTCT | GCAAACTGAC | ATTAAATTCT | AGATGTTGAC | AATTACTGAA | TCAGAAGGCA | 1260 |
| | TGAAAGAGTA | TAATTTTAT G | АААТТСАААА | TTATTCTTTT | TTCAAGTTGA | AACTTGCCTC | 1320 |
| 20 | TTCTACTTTA | AA AA AGTATA | TAGAACAG T T | ACTTCTAATA | ATCAGAAAGA | GATGTTTTAT | 1380 |
| 20 | AGAACATTTC | TTTAATATAA | AGTTAGAGAT | GTCTTCATAG | GCAGTATGGC | TATCTTTGCC | 1440 |
| | ACAGAAACAT | AAGTAAAATT | TTAGAGTTCT | GTTTTCCATG | AGGTCAAAAA | TATAATTTAT | 1500 |
| 25 | TCCTCAGTCA | TGGTTTTCTA | AATATCTGTA | CTCCACATTC | CATTTTAATT | GATATGAGGG | 1560 |
| | TGTTAAAGTA | CCTACTTAAT | GGGTTGATTA | CTATCAAAAT | GACCAAATTA | TACCAAAGAA | 1620 |
| 30 | CTTAAGAGGA | AGCACTTTCA | GAACTATTCA | CTTGCCAGGT | ATTTTCTAAA | ATTCCACCTG | 1680 |
| 30 | AAAGCCAAAA | GATAAAATAC | ATNAGTTGGA | TTTTAATGAT | ATAAGCATCA | CACAATTTTA | 1740 |
| | CATTAAGAAA | TACTGTGCAG | CCCATGCGTG | GTGGCTCAGG | CCTGTAATCC | CAGCANTTTG | 1800 |
| 35 | GGAGGCCGAG | GTGGGCAGAT | CACCGGAGGT | CAGGAGTTCG | AGACCAGCCT | TGCCAACATA | 1860 |
| | GTGAAACCCT | GTCTTTACTA | ААААТАСААА | AATTAGCCGG | GCATGGTGGC | AGGCACCTGT | 1920 |
| 40 | AATCCCAGCT | ACTAGGGAGG | CTTTTGAACC | CAGGAGGCAG | AGGTTGCAGC | GAGCTGAGAT | 1980 |
| -10 | CGCGCCACTG | CACTCCAGCC | TGGGTGATAG | AGTGAGATTC | AGTCTCAAAA | AAAAAAAA | 2040 |
| | АААААААА | AATGACCTCG | A | | | | 2061 |
| 45 | | | | | | | |
| | (2) INFORM | ATION FOR S | EO ID NO: 1 | .5 : | | | |
| 50 | | SEQUENCE (| | | | | |
| 30 | (1) | (A) LE | NGTH: 1412 PE: nucleic | oase pairs | | | |
| | | (C) ST | RANDEDNESS: POLOGY: line | double | | | |
| 55 | / | , | | N: SEQ ID NO | or 15: | | |
| | , | | | - | | CATCCTTGCC | 60 |
| | CCCITCMICI | COLICCA | | | | | • |

AGGAAGCTCT GTGAAGGTGC TGCTGATGAC CCAGATTCCT CCATGGTCCT CCTGTGTCTC

| | CTGTTGGTGC | CCCTCCTGCT | CAGTCTCTTT | GTACTGGGGC | TATTTCTTTG | GTTTCTGAAG | 180 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | AGAGAGAGAC | AAGAAGAGTA | CATTGAAGAG | AAGAAGAGAG | TGGACATTTG | TCGGGAAACT | 240 |
| 3 | CCTAACATAT | GCCCCCATTC | TGGAGAGAAC | ACAGAGTACG | ACACAATCCC | TCACACTAAT | 300 |
| | AGAACAATCC | TAAAGGAAGA | TCCAGCAAAT | ACGGTTTACT | CCACTGTGGA | AATACCGAAA | 360 |
| 10 | AAGATGGAAA | ATCCCCACTC | ACTGCTCACG | ATGCCAGACA | CACCAAGGCT | ATTTGCCTAT | 420 |
| | GAGAATGTTA | TCTAGACAGC | AGTGCACTCC | CCTAAGTCTC | TGCTCAAAAA | АААААСААТТ | 480 |
| 15 | CTCGGCCCAA | AGAAAACAAT | CAGAAGAATT | CACTGATTTG | ACTAGAAACA | TCAAGGAAGA | 540 |
| 13 | ATGAAGAACG | TTGACTTTTT | TCCAGGATAA | ATTATCTCTG | ATGCTTCTTT | AGATTTAAGA | 600 |
| | GTTCATAATT | CCATCCACTG | CTGAGAAATC | TCCTCAAACC | CAGAAGGTTT | AATCACTTCA | 660 |
| 20 | TCCCAAAAAT | GGGATTGTGA | ATGTCAGCAA | ACCATAAAAA | AAGTGCTTAG | AAGTATTCCT | 720 |
| | ATAAAAATGT | AAATGCAAGG | TCACACATAT | TAATGACAGC | CTGTTGTATT | AATGATGGCT | 780 |
| 25 | CCAGGTCAGT | GTCTGGAGTT | TCATTCCATC | CCAGGGCTTG | GATGTCAGGA | TTATACCAAG | 840 |
| 23 | AGTCTTGCTA | CCAGGAGGGC | AAGAAGACCA | AAACAGACAG | ACAAGTCCAG | CAGAAGCAGA | 900 |
| | TGCACCTGAC | AAAAATGGAT | GTATTAATTG | GCTCTATAAA | CTATGTGCCC | AGCAYTATGC | 960 |
| 30 | TGAGCTTACA | CTAATTGGTC | AGACATGCTG | TCTGCCCTCA | TGAAATTGGC | TCCAAATGAW | 1020 |
| | TGAACTACTT | TCATGAGCAG | TTGTAGCAGG | CCTGACCACA | GATTCCCAGA | GGGCCAGGTG | 1080 |
| 35 | TGGATCCACA | GGACTTGAAG | GTCAAAGTTC | ACAAAGATGA | AGAATCAGGG | TAGCTGACCA | 1140 |
| ,, | TGTTTGGCAG | ATACTATAAT | GGAGACACAG | AAGTGTGCAT | GGCCCAAGGA | CAAGGACCTC | 1200 |
| | CAGCCAGGCT | TCATTTATGC | ACTTGTCTGC | AAAAGAAAAG | TCTAGGTTTT | AAGGCTGTGC | 1260 |
| 40 | CAGAACCCAT | CCCAATAAAG | AGACCGAGTC | TGAAGTCACA | TTGTAAATCT | AGTGTAGGAG | 1320 |
| | ACTTGGAGTC | AGGCAGTGAG | ACTGGTGGGG | CACGGGGGGC | ANTGGGTANT | GTAAACCTTT | 1380 |
| 45 | TAAAGATGGT | TAATTCNTCA | TTAGTGTTTT | TT | | | 1412 |
| | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 16: 50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1052 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

TTCCTCTCT CTCTCTACCC CTCCTGTCTC TCCTCCCCTC CTCTCTCTC CTCTCCTCTC 60

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| | TCTCTTCCTC TCCTCTCTT TCCCTTCCTG TCTCTCTTCC CCTCCTCTCT CTCTTCCTGT | 120 |
|-----|---|-------------|
| | CCTCTATCTC TTCCCCTCCT CTATCTCTTC CTCTCCTCTC TCTCTTCCTC TCCTCTCTCT | 180 |
| 5 | CTCTTSCTTT CTTCTCTCT TCCTGTCTCG GCTGTTGTGG GTTGCAGGTT GGGTGCTGCT | 240 |
| | GTTGTGGTCC TTCCCAGAAA CTGCCAGTAG AGGGCAGCCT GGGCATCCTA ATGCTTACTC | 300 |
| 10 | TGGTTGTTAC ACAAAGAAAA TATTGGGGTC ACTGGCGAGC CCACCCACAC TCACCAGAAT | 360 |
| 10∠ | CTCCACTGTA GTCCCCCTAA CAAACAGCCC TTCACTTCCT CTCCCACTTC AGCAATTTGT | 420 |
| | ATTTGATGC CATTGGCCTC AGATCAGAGT GTTTTAAATC ATCACGCCCT GGCTTATCCC | 480 |
| 15 | TGGTCGAGCC AGGACACGGG GTGCTTCAGT GGGTCTGTCA CCCTCTCTCC TTGAAGCATG | 540 |
| | TTGCTTTTAT TTATTTACTT TTACTCTCAC CCTGCTCCTG TACCAGCAGG GGCCACTTCA | 600 |
| 20 | AAGCCAAGGT ACAGGGTGAT AACTTGTGGT CCAGCATCAG TTTTCTCCAC TTCTTTCTCC | 660 |
| 20 | CACTCACCCC CAGCAAGGTG CCTGGGGAGA CTTGAGCAGA TGTTTCATTT TGGCCTGGCC | 720 |
| | AGTGGCTGAA AGCAGGCCTC CAATGCACTG TGACCTCTGG CTTCCCCAGC AGCTTTCCCA | 7 80 |
| 25 | GAGAGGCAGA GGGGCCTTCC ACAGCCCGGG TTCTCCTGCT GCCTCCTGCC TGCTGCAGCT | 840 |
| | GCAGGCATTC TGAGGGCAA CGTGGAGGAA GGGCCAGGGA TGCATGGGAT TTTAATTGTT | 900 |
| 30 | TCATCACACC TTCCCCGTGG CAAAGAAACA GTCAGTCCTC TTCAGGTGTC TTCTGGATTT | 960 |
| 30 | CTGGTGATGG ACAGAGAAAT CTTTTTACAG TTTCAAATTA TGTTCAACAA ATAAAAATTG | 1020 |
| | CATTTTTAT TTTGGAAAAA AAAAAAAAAA AA | 1052 |
| 35 | | |
| | (2) INFORMATION FOR SEQ ID NO: 17: | |
| 10 | | |
| 40 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 683 base pairs | |
| | (B) TYPE: nucleic acid(C) STRANDEDNESS: double | |
| 45 | (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17: | |
| | AATTCGGCAG AGGCACTTAT CATGTACATA TAGCCTGTTT TTTAGCATTG TTAGACAAAG | 60 |
| 50 | TAGGCATATT CCTTTCCATC CAAGAACTCA TAACCTAGTA ATTGTAGTTG GCTGATAGCT | 120 |
| | CATTGCCCAT ACACAAGGAT CTAACACAAC CTCTTGAATA AACATCCCCC TTATTCAGAA | 180 |
| 55 | ATGCCTTTC CTATTTCCAT ATTGCAACTT TGCTTACAAA TTTCCAATCT GTCTTTCTGT | 240 |
| 55 | TTACAGAAGA TATACAAAAT TCCTTTTGTA TGATCTCTTT ATATCTCTTG ATTTTCTTTT | 300 |

GTGTTTGCTA CCAAAGGGCC TGCACATAGT GAGAAGATTG TGCATGATCT GTGAGCTCTA

CCACACCTGG AATTAGGGAT CACCAATATG AGAAAAAAA TTGGAGGTAC AAATAACATT

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| | ATCATATGTW | ATTGGCATAT | AAATTACAGA | TGTWICTATG | ACTAAAAACC | CTGTGGATAT | 480 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 5 | WAACCMAATG | CAGATAAWIW | WTAAAAATW | WTAAAAATW | TWATCMAATA | ATGATAGTGC | 540 |
| J | TATTCAAATA | CTTCAAATTT | GCACAGTGAT | TTATTTCTTA | AAATATGTTA | ACACATGTGA | 600 |
| | GCCAATACAC | TGAGGTCACT | GGATAAATAA | ACAGATTCTT | GCAAAAAAAA | AAAAAAAA | 660 |
| 10 | ACTCGAGGGG | GGCCCGTACC | CTT | | | | 683 |

15 (2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1054 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

| 25 | AAACTCATTT | AGGTGACACT | ATAGAAGGTA | CGCCTGCAGG | TACCGGTCCG | GAATTCCCGG | 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GTCGACCCAC | GMGNCCGGCG | ACAAGATGGC | AGCAGCGTGT | CGGAGCGTGA | AGGGCCTGGT | 120 |
| 30 | GGCGGTAATA | ACCGGAGGAG | CCTCGGGCCT | GGGCCTGGCC | ACGGCGGACG | ACTTGTGGGG | 180 |
| 50 | CAGGGAGCCT | CTGCTGTGCT | TCTGGACCTG | CCCAACTCGG | GTGGGGAGGC | CCAAGCCAAG | 240 |
| | AAGTTAGGAA | ACAACTGCGT | TTTCGCCCCA | GCCGACGTGA | CCTCTGAGAA | GGATGTGCAA | 300 |
| 35 | ACAGCTCTGG | CTCTAGCAAA | AGGAAAGTTT | GGCCGTGTGG | ATGTAGCTGT | CAACTGTGCA | 360 |
| | GGCATCGCGG | TGGCTAGCAA | GACGTACAAC | TTAAAGAAGG | GCCAGACCCA | TACCTTGGAA | 420 |
| 40 | GACTTCCAGC | GAGTTCTTGA | TGTGAATCTC | ATGGGCACCT | TCAATGTGAT | CCGCCTGGTG | 480 |
| .0 | GCTGGTGAGA | TGGGCCAGAA | TGAACCAGAC | CAGGGAGGCC | AACGTGGGGT | CATCATCAAC | 540 |
| | ACTGCCAGTG | TGGCTGCCTT | CGAGGGTCAG | GTTGGACAAG | CTGCATACTC | TGCTTCCAAG | 600 |
| 45 | GGGGGAATAG | TGGGCATGAC | ACTGCCCATT | GCTCGGGATC | TGGCTCCCAT | AGGTATCCGG | 660 |
| | GTGATGACCA | TTGCCCCAGG | TCTGTTTGGC | ACCCCACTGC | TGACCAGCCT | CCCAGAGAAA | 720 |
| 50 | GTGTGCAACT | TCTTGGCCAG | CCAAGTGCCC | TTCCCTAGCC | GACTGGGTGA | CCCTGCTGAG | 780 |
| 50 | TATGCTCACC | TCGTACAGGC | CATCATCGAG | AACCCATTCC | TCAATGGAGA | GGTCATCCGG | 840 |
| | CTGGATGGG | CCATTCGTAT | GCAGCCTTGA | AGGGAGAAGG | CAGAGAAAAC | ACACGCTCCT | 900 |
| 55 | CTGCCCTTCC | TTTCCCTGGG | GTACTACTCT | CCAGCTTGGG | AGGAAGCCCA | GTAGCCATTT | 960 |
| | TGTAACTGCC | TACCAGTCGC | CCTCTGTGCC | TAATAAAGTC | TCTTTTTCTC | ACANAAAAA | 1020 |
| 60 | АААААААА | АААААААА | AAAAAAAA | AAAA | | | 1054 |

5 .

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1393 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

10

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

| . 5 | GGAACAAGCT | GGGATATGTG | AGCGTTAAGC | TACTCACATC | CTTCAAAAAG | GTGAAACATC | 60 |
|-----|-------------|--------------|------------|-------------|--------------|--------------|------|
| 15 | TTACACGGGA | CTGGAGAACC | ACAGCACATG | CTTTGAAGTA | TTCAGTGGTC | CTTGAGTTGA | 120 |
| | ATGAGGNCCA | CCGGAAGGTG | AGGAGGACCA | CCCCCGTCCC | ACTGTTCCCC | AACGAGAACC | 180 |
| 20 | TCCCCAGCAA | GATGCTCCTG | GTCTATGATC | TCTACTTGTY | TCCTAAGCTG | TGGGCTCTGG | 240 |
| | CCACCCCCA | GAAGAATGGG | AAGGGTGCAA | GARAAGGTGA | TGGAACACCT | GCTCAAGCTT | 300 |
| 25 | TTTGGGACTT | TTGGAGTCAT | CTCATCAGTG | CGGATCCTCA | AACCTGGGAG | AGAGCTGCCC | 360 |
| 23 | CCTGACATCC | GGAGGNTCCA | GCAGCCGCTA | CAGCTCCTCT | GACCCCGAGA | GCAACCCCAC | 420 |
| | ATCCCCTATG | GCGGGCCGAC | GGCACGNGKC | CACCAACAAG | CTCAGCCCGT | CTGGCCACCA | 480 |
| 30 | GAATCTCTTT | CTGAGTCCAA | ATGCCTCCCC | GTGCACAAGT | CCTTGGAGCA | GCCCCTTGGC | 540 |
| | CCAACGCAAA | GGCGTTTCCA | GAAAGTCCCC | ACTGGCGGAG | GAAGGTAGAC | TGAACTGCAG | 600 |
| 25 | CACCAGCCCT | GAGATCTTCC | GCAAGTGTAT | GGATTATTCC | TCTGACAGCA | GCGTCACTCC | 660 |
| 33 | CTCTGGCAGC | CCCTGGGTCC | GGAGGCGTCG | CCAAGCCGAG | ATGGGGACCC | AGGAGAAAAG | 720 |
| | CCCCGGTACG | AGTCCCCTGC | TCTCCCGGAA | GATGCAGACT | GCAGATGGGS | TACCCGTAGG | 780 |
| 40 | TNGCTTGAGG | TTGCCCAGGG | GTCCTGACAA | CACCAGAGGA | TTTCATGGCC | ATGAGAGGAG | 840 |
| | CAGGGCCTGT | GTATAAATAC | CTTCTATTTT | TAATACAAGO | TCCACTGAAA | ACCACCTTCG | 900 |
| 45 | TTTTCAAGGT | TCTGACAAAC | ACCTGGCATG | ACAGAATGGA | ATTCGTTCCC | CTTTGAGAGA | 960 |
| 43 | TTTTTTTATTC | : ATGTAGACCT | CTTAATTTAT | CTATCTGTA | A TATACATAAA | TCGGTACGCC | 1020 |
| | ATGGTTTGAA | GACCACCTTC | TAGTTCAGGA | CTCCTGTTCT | TCCCAGCATO | GCCACTATTT | 1080 |
| 50 | TGATGATGGC | TGATGTGTGT | GAGTGTGATC | GCCCTGAAGO | GCTGTAGGAC | GGAGGTTCCC | 1140 |
| | TGGGGGAAGT | CTGTTCTTTC | GTATGGAATT | TTTCTCTCT. | r ctttggtate | GAATTTTTCC | 1200 |
| 55 | CTTCAGTGAG | TGAGCTGTC | TCGATAGGC | C ATGCAAGGG | C TTCCTGAGA | G TTCAGGAAAG | 1260 |
| 33 | TTCTCTTGTC | G CAACAGCAAG | TAGCTAAGC | TATAGCATG | G TGTCTTGTA | G GACCAAATCG | 1320 |
| | ATGTTACCT | G TCAAGTAAA | AATAATAA | A ACACCCAAC | T GGGAGTGCTY | AAAAAAAANA | 1380 |
| 60 | ANNAAAAAA | C TCG | | | | | 1393 |

5 (2) INFORMATION FOR SEQ ID NO: 20:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1215 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

| | (302) | | | | | | |
|----|------------|------------|------------|------------|------------|------------|------|
| 15 | AGGAAAAGTT | TTCCNAATTG | GAAAGCGGGC | AGTGAGCGCA | ACGCAATTAA | TGTGAGTTAG | 60 |
| | NTCANTCATT | AGGCACCCCA | GGCTTTACAC | TTTATGCTTC | CGGNTCGTAT | GTTGTGTGGA | 120 |
| 20 | ATTGTGAGCG | GATAACAATT | TCACACAGGA | AACAGCTATG | ACCATGATTA | CGCCAAGCTN | 180 |
| 20 | TAATACGACT | CACTATAGGG | AAAGCTGGTA | CGCCTGCAGG | TACCGGTCCG | GAATTCCCGG | 240 |
| | GTCGACCCAC | GCGTCCGCCC | ACGCGTCCGT | GAAAATCCGA | AGTGCCGCGG | AAAGTGGAGG | 300 |
| 25 | TGAGGGCCGC | CCGCCCTAGA | GGTGCCCGTC | CGAGAGGCAG | AGCTGACAAG | GAAGGTTTCG | 360 |
| | AGCGTTTTGC | TGGCAAAGGG | ATTTCTTACA | ACCTCCAGGC | ATGCGTCTTT | CTGCCCTGCT | 420 |
| 30 | GGCCTTGGCA | TCCAAGGTCA | CTCTGCCCCC | CCATTACCGC | TATGGGATGA | GCCCCCAGG | 480 |
| 50 | CTCTGTTGCA | GACAAGAGGA | AGAACCCCCC | ATGGATCAGG | CGGCGCCCAG | TGGTTGTGGA | 540 |
| | ACCCATCTCT | GATGAAGACT | GGTATCTGTT | CTGTGGGGAC | ACGGTGGAGA | TCCTAGAAGG | 600 |
| 35 | CAAGGATGCC | GGGAAGCAGG | GCAAAGTGGT | TCAAGTTATC | CGGCAGCGAA | ACTGGGTGGT | 660 |
| | CGTGGGAGGG | CTGAACACAC | ATTACCGCTA | CATTGGCAAG | ACCATGGATT | ACCGGGGAAC | 720 |
| 40 | CATGATCCCT | AGTGAAGCCC | CCTTGCTCCA | CCGCCAGGTC | AAACTTGTGG | ATCCTATGGA | 780 |
| •• | CAGGAAACCC | ACTGAGATCG | AGTGGAGATT | TACTGAAGCA | GGAGAGCGGG | TACGAGTCTC | 840 |
| | CACACGATCA | GGGAGAATTA | TCCCTAAACC | CGAATTTCCC | AGAGCTGATG | GCATCGTCCC | 900 |
| 45 | TGAAACGTGG | ATTGATGGCC | CCAAAGACAC | ATCAGTGGAA | GATGCTTTAG | AAAGAACCTA | 960 |
| | TGTGCCCTGT | CTAAAGACAC | TGCAGGAGGA | GGTGATGGAG | GCCATGGGGA | TCAAGGAGAC | 1020 |
| 50 | CCGGAAATAC | AAGAAGGTCT | ATTGGTATTG | AGCCTGGGGC | AGAGCAGCTC | CTCCCCAACT | 1080 |
| 50 | TCTGTCCCAG | CCTTGAAGGC | TGAGGCACTT | CTTTTTCAGA | TGCCAATAAA | GAGCACTTTA | 1140 |
| | TGAGTCCTCC | AAAAAAAA | AAAAAAAA | AAAAAAAAA | AAAAAAAA | АААААААА | 1200 |
| 55 | AAAAGGGGCG | GCCGC | | | | | 1215 |

60 (2) INFORMATION FOR SEQ ID NO: 21:

5

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2042 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

CTGCATCCAG GCGCAGAATA ACCTGGGTAT CTTGTGGTCT GAAAGAGAGA AATTGAAACT

| | GCACAGGCTT ACCTAGAGTC ATCAGAAGCA CTATATAATC AGTATATGAA AGAGGTTGGC | G 120 |
|----|---|---------|
| 15 | AGTCCTCCTC TTGATCCTAC TGAGCGTTTT CTTCTGAAGA AGAGAAACTT ACTGAACAAC | G 180 |
| 13 | AGAGATCAAA AAGATTTGAA AAGGTTTATA CTCATAACCT ATATTACCTA GCTCAAGTC | r 240 |
| | ACCAGCATCT GGAAATGTTT GAGAAGGCTG CTCACTATTG CCATAGTACA CTAAAACGC | 300 |
| 20 | AGCTTGAGCA CAATGCCTAC CATCCTATAG AGTGGGCTAT CAATGCTGCT ACCTTGTCA | 360 |
| | AGTTTTACAT CAATAAGCTA TGCTTTATGG AGGCCAGGCA CTGTTTATCA GCTGCTAAT | G 420 |
| 25 | TCATTTTTGG TCAAACTGGA AAGATCTCAG CCACAGAAGA CACTCCTGAA GCTGAAGGA | G 480 |
| 23 | AAGTGCCAGA GCTTTATCAT CAAAGAAAGG GGGAAATAGC AAGGTGCTGG ATCAAATAC | r 540 |
| | GTTTGACTCT CATGCAGAAT GCCCAACTCT CCATGCAGGA CAACATAGGA GAGCTTGAT | C 600 |
| 30 | TTGATAAACA GTCTGAACTT AGAGCTTTAA GGAAAAAAGA ACTAGATGAG GAGGAAAGC | A 660 |
| | TTCGGAAAAA AGCTGTGCAG TTTGGAACCG GTGAACTGTG TGATGCCATC TCTGCAGTA | G 720 |
| 35 | AAGAGAAAGT GAGCTACTTG AGACCTTTAG ATTTTGAAGA AGCCAGAGAA CTTTTCTTA | т 780 |
| 33 | TGGGTCAGCA CTATGTCTTT GAGGCAAAAG AGTTCTTTCA GATTGATGGT TATGTCACT | G 840 |
| | ACCATATTGA AGTTGTCCAA GACCACAGTG CTCTGTTTAA GGTGCTTGCA TTCTTTGAA | A 900 |
| 40 | CTGACATGGA GAGACGGTGC AAGATGCATA AACGCRGAAT AGCCATGCTA GAGCCCCTA | A 960 |
| | CTGTAGACCT GAATCCACAG TATTATCTGT TGGTCAACAG ACAGATCCAG TTTGAAATT | G 1020 |
| 45 | CACATGCTTA CTATGATATG ATGGATTTGA AGGTTGCCAT TGCTGACAGG CTAAGGGAT | °C 1080 |
| 45 | CTGATTCACA CATTGTAAAA AAAATAAATA ATCTTAATAA GTCAGCACTG AAGTACTAC | CC 1140 |
| | AGCTCTTCTT AGACTCCCTG AGAGACCCAA ATAAAGTATT CCCTGAGCAT ATAGGGGAA | AG 1200 |
| 50 | ATGTTCTTCG CCCTGCCATG TTAGCTAAGT TTCGAGTTGC CCGTCTCTAT GGCAAAATC | A 1260 |
| | TTACTGCAGA TCCCAAGAAA GAGCTGGAAA ATTTGGCAAC ATCATTGGGA ACATTACAA | AA 1320 |
| 55 | TTTATIGTTG ATTACTGTGA AAAGCATCCT GAGGCCGCCC AGGAAATAGA AGTTGAGCT | ra 1380 |
| 33 | GAACTTAGTA AAGAGATGGT TAGTCTTCTC CCAACAAAAA TGGAGAGATT CAGAACCAA | AG 1440 |
| | ATGGCCCTGA CTTAATCCTT GTTTTTAAAG AAAGGAAATG TGCAATATTG AAGTGATCT | rr 1500 |
| 60 | TTTCCCTAGT CAGACAGGCC CAATTCCATT GTGATGTTTA CCTTTATAGC CAGGTGAG | rg 1560 |

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| | CAGTTTGAAC TTGAGATACA GTCAACTGAG TGTTTGCTAG GATCCTAAGG AACATAAAGT | 1620 |
|----------|---|------|
| 5 | TAATTAAAAA CTTACACCTA ATTATGTAAA TTGCCTTGTT AAAGACATGT GATTTGTATT | 1680 |
| <i>3</i> | TTAGATGCTT GTTTCCTATT AAAATACAGA CATTTCTACC CTCAGTTTCT AAATGTAGAC | 1740 |
| | TATTTGTTGG CTAGTACTTG ATAGATTCCT TGTAAGAAAA AATGCTGGGT AATGTACCTG | 1800 |
| 10 | GTAACAAGCC TGTTAATATA TTAAGATTGA AAAAGTAACT TCTATAGTTA CTCCTTCTAA | 1860 |
| | AATATTTGAC TTCCTACATT CCCCCCACCC AAAATCTTTC CCTTTTGAAA ATACTAAAAA | 1920 |
| 1.5 | CTAAGTTATG TTATTATAAA GTGTAAAATG GTTTGTCTTA ATTATAGGAG AAAAAGGCCT | 1980 |
| 15 | TGTTAGAAAT AAAATAAACT GACTTATTTC ACTAATGAAA AAAAAAAAA AAAAAAAAA | 2040 |
| | TT | 2042 |
| 20 | | |
| | | |
| | (2) INFORMATION FOR SEQ ID NO: 22: | |
| 25 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1872 base pairs | |
| | (B) TYPE: nucleic acid (C) STRANDEDNESS: double | |
| 30 | (D) TOPOLOGY: linear | |
| 50 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22: | |
| | GGGTCGACCC ACGCGTCCGA TTGGCCTAGA GCTCCTGTGA CCGAGAGCGC CACGGAAGCC | 60 |
| 35 | TGGGGATGAT GTCGGGCAGC TTTATTCTTT GCTTGGCTTT GGTAACTAGG TGGTCCCCTC | 120 |
| | AAGCATCCTC AGTTCCTCTT GCTGTTTATG AATCTAAGAC AAGGAAGTCC TATAGAAGCC | 180 |
| 40 | AAAGGGACAG GGACGGAAAG GACAGGTCCC AAGGGATGGG GCTGTCTTTA CTTGTGGAAA | 240 |
| 10 | CCAGGAAATT GCTCCTCTCA GCCAACCAAG GTTGACCACA CACCACCCTT CCGGAGCAGC | 300 |
| | TCAGTCAGCC CTCGGGGACG RGAAACCACA AGCGCAGAGA CGCTGAGGCC CAGGCAGGTG | 360 |
| 45 | AAGAGGAAGT GGCTTTGGGT TTTTAAAGTA GGTGAGCGTG ACCTCTCTGA CTGCTTCTTC | 420 |
| | CCCGGGGGGG ACTGCAAACC GCTCAGGGTT GCGGCAGAGC CATGGACTTC CGGTCCCTGC | 48 |
| 50 | AACGGGTGAC CTAAGCGTGG TGCACCCATC AGTCACGCAG GAGGACTGAC TTGACAGACG | 54 |
| 50 | AAAGACAAGC CCGGATGACA CAGGGTGAGA AGAGTCAGGG CCGCACCTCT GTCCCTGCAA | 60 |
| | ACCAACAGGT GCATGGTGAG TGTGGCAGTC CCCACAGCTC CACAATGGGC TCCCCCGCCA | 66 |
| 55 | ACGGGGACGA CAGGGATCTT CAGGAACTTC TGACCTCACC AAGTCAAGTG GACCACTCTC | 72 |
| | CACTCCACGA GGATGTGAAA CGGTTCTTTA AAATGGGATT TTAGAGCCTC GGGAATGCAT | 78 |

GTGCGTCGCA TCTTTCATAT TATGGGTCAG GATAGATTCA TTTCTTGCAA CATAGTGGAA

840

179

| | AAGATATAAG | CTGCAGTAAT | TTGCTCTTTG | AATGACCGTC | ACCCCCAGTA | TAGGATATGC | 900 |
|-----|------------|------------|------------|------------|------------|------------|--------|
| | TTGTATCCCC | CCGTCACTCC | TCCGCCTGTT | TTTTAAACTT | TTCCACCACC | TGCGTCCAAA | 960 |
| 5 | AAGAATGTTA | TAGCGAGTGC | TCTTAAATGT | TGAACCTGGG | TGTTGCTTCC | GGGCCAGTCT | 1020 |
| | GCGTGGCTCC | ATGAAAAGCT | CACTGCTGCC | CCAGCCGGGC | TTCTTAGAGG | AGGTCAGTTG | 1080 |
| • • | TCCTATGTAT | CATCATTTAC | TCTGGGAATC | CTACTGTGAA | ATCATGTCTG | TATTTTTCTG | 1140 |
| 10 | GAGCAGTTCA | CATAGAGTAG | AATGTGGAAT | TTCCCGTGAA | CGTCTCCTTC | CTCCCCGTA | 1200 |
| | TCTGCCGCCT | GTCACTTCGC | CACCGTGCTA | GAATACTGTT | GTGTTGTAAG | ATGACTAATT | , 1260 |
| 15 | TTAAAAGAAC | CTGCCCTGAA | AAGTTCTTAG | AAACGCAATG | AAAGGGAGGA | ACTIGICCTT | 1320 |
| | TACCCAGTTT | TTCCTTTGTA | GGATGGGAAA | GTATAAAAAG | GCACAGAAGG | TTGTCATGGG | 1380 |
| | CTGTTCCTTG | GGGTTTTTA | TCCTGCTCAC | CGTGGAGATA | AGCCTGCGGC | TTGTCTAACC | 1440 |
| 20 | AGCGCAGCGM | AAAGGTCTCA | ATGCCTTTTG | GTAACATCCG | TCATTGCAGA | AGAAAGTTTA | 1500 |
| | CACGACGTCA | AAAAGTGACG | TTCATGCTAA | GTGTTTTTCC | AGAAATATTG | GTTTCATGTT | 1560 |
| 25 | TCTTATTKGC | TCTGCCTCCT | GTGCTTATAT | САТССААААА | СТТТТТАААА | AGGTCCAGAA | 1620 |
| | TTCTATTTTA | ACCTGATGTT | GAGCACCTTT | AAAACGTTCG | TATGTGTGTT | GCACTAATTC | 1680 |
| •• | TAAACTTTGG | AGGCATTTTG | CTGTGTGAGG | CCGATCGCCA | CTGTAAAGGT | CCTAGAGTTG | 1740 |
| 30 | CCTGTTTGTC | TCTGGAGATG | GAATTAAACC | AAATAAAGAG | CTTCCACTGG | AGGCTTGTAT | 1800 |
| | TGACCTTGTA | ACTATATGTT | AATCTCGTGT | ТААААТАААТ | TATAACTTGT | GAAAAAAAA | 1860 |
| 35 | дааааааас | NT | | | | | 1872 |

40 (2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 289 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

50 CATTTACCCA CCTATCAACA TGTTTGCTTT CTCTTTTGTT GGTGAGAATG AGTGGCTTCT 60

TGCTCCTAGC TAGAGCCAGT CCTTCCATAT GTGCTTTAGA TTCTTCCTGT TTTGTTCAAG 120

AATATTGCTC AAGCTATTCT TCCTCCTGTT TCCTGCATCA GCATTTCCCC TCTCTACTAG 180

ATCATCTCTG TCAGTAAATG AACATGTTGT TGTTTCTCCT AGAAGTACTG TTTCTATATC 240

TAGATAGTAC TCTAGCTAGA GTTAAAAAAA AAAAAAAAA CCTNGGGGG 289

60

(2) INFORMATION FOR SEQ ID NO: 24:

| 5 | (i) | (B) TYPE: (C) STRAN | RACTERISTI TH: 3533 ba nucleic a DEDNESS: C LOGY: linea | ase pairs acid double | | | |
|----|------------|------------------------|---|-----------------------------|------------|------------|------|
| 10 | (xi) | SEQUENCE DE | SCRIPTION: | SEQ ID NO: | 24: | | |
| | TTTTATTTAC | ттсаааттаа с | TGTACTTTA | CTCAAATAGA | AAANGAATAA | TTTTCACATT | 60 |
| 15 | ATGAAGCTAC | ACAATTCCAA A | ATACACATG | CTGAGGCTCT | TTTTAAGTCC | GAATTGTCTA | 120 |
| | GTAATTACAA | AAAAGTGAAG A | GTTTACAGA | TATACAAGGA | AATAAAGGCG | AATTATTGCA | 180 |
| 20 | AAGAAAACAA | GTTTAATTTC A | CTTTGAATG | ACAACGATTT | TTCTGGAAAG | CAGATACTTC | 240 |
| | ACTCCTTTAA | GTTTCCACCC A | AGCCACAAT | AATTTCAAAC | GGTCTTGCGG | ATGACCCAGC | 300 |
| | TGGTCACTCT | TGTTTATGTG G | GGACTGGAG | GTAATGAGAG | CCAAAAAAAG | TGCTATAAAC | 360 |
| 25 | CTAATTIGGC | TAGAGCAAGT T | CACACGACA | CGACCGTGCT | TTAAAAACTT | GCTCTCCATT | 420 |
| | ATGTACTTCC | TTCCATCAGG T | TGGGGAAAA | AAAAATGGTG | GGGATGGTGA | GTAAACACAC | 480 |
| 30 | CAGTGGTTTC | ATCAGAGGGG A | ACTCACTAC | TCAGGAGGTG | ACGGTGACGT | GGTGCCGGTC | 540 |
| | CCTGAAGTAC | GCGCACAAGC T | CCGGAGGTT | GCGGGAGCTT | CCGCTGCCGC | CTGGAGGGAA | 600 |
| | GCCGGAGCGA | CGGGGTCAC G | GCGGCGGTC | AGAGGGTAAA | GGTCTTGCTC | CCAGCAGCCT | 660 |
| 35 | CCGCGGTGGA | TACGTCGCCA I | CTTGGATCC | GCGGGACAAG | AAAATTCATG | CGAGGGAGAC | 720 |
| | GTGGTGGGCG | GTCCTTCCTG I | GACACGACC | CTTGAGTGAC | AGTTCTATTT | GATTGCCTCC | 780 |
| 40 | GGTACTGTGA | GGAAAGGACA C | GACTCTATG | GTGAGGACTG | ATGGACATAC | ATTATCTGAG | 840 |
| | AAAAGAAACT | ACCAGGTGAC A | AACAGCATG | TTTGGTGCTT | CAAGAAAGAA | GTTTGTAGAG | 900 |
| | GGGGTCGACA | GTGACTACCA T | GACGAAAAC | ATGTACTACA | GCCAGTCTTC | TATGTTTCCA | 960 |
| 45 | CATCGGTCAG | AAAAAGATAT C | CTGGCATCA | CCATCTACAT | CAGGTCAGCT | GTCTCAGTTT | 1020 |
| | GGGGCAAGTT | TATACGGGCA A | ACAAAGTGCA | CTAGGCCTTC | CAATGAGGGG | GATGAGCAAC | 1080 |
| 50 | AATACCCCTC | AGTTAAATCG (| CAGCTTATCA | CAAGGCACTC | AGTTACCGAG | CCACGTCACG | 1140 |
| | CCAACAACAG | GGGTACCAAC A | AATGTCACTT | CACACGCCTC | CATCTCCAAG | CAGGGGTATT | 1200 |
| | TTGCCTATGA | ATCCTARGAA 7 | PATGATGAAC | CACTCCCAGG | TTGGTCAGGG | CATTGGAATT | 1260 |
| 55 | CCTAGCAGGA | CAAATAGCAT (| GAGCAGTTCA | GGGTTAGGTA | GCCCCAACAG | AAGCTCGCCA | 1320 |
| | AGCATAATAT | GTATGCCAAA (| GCAGCAGCCT | TCTCGACAGC | CTTTTACTGT | GAACAGTATG | 1380 |
| 60 | TCTGGATTTG | GAATGAACAG (| GAATCAGGCA | TTTGGAATGA | ATAACTCCTT | ATCAAGTAAC | 1440 |

| | ATTTTTAATG | GAACAGACGG | AAGTGAAAAT | GTGACAGGAT | TGGACCTTTC | AGATTTCCCA | 1500 |
|----|------------|------------|------------|--------------|---------------------|------------|------|
| | GCATTAGCAG | ACCGAAACAG | GAGGGAAGGA | AGTGGTAACC | CAACTCCATT | AATAAACCCC | 1560 |
| 5 | TTGGCTGGAA | GAGCTCCTTA | TGTTGGAATG | GTAACAAAAC | CAGCAAATGA | ACAATCCCAG | 1620 |
| | GACTTCTCAA | TACACAATGA | AGATTTTCCA | GCATTACCAG | GCTCCAGCTA | TAAAGATCCA | 1680 |
| 10 | ACATCAAGTA | ATGATGACAG | TAAATCTAAT | TTGAATACAT | CTGGCAAGAC | AACTTCAAGT | 1740 |
| 10 | ACAGATGGAC | CCAAATTCCC | TGGAGATAAA | AGTTCAACAA | CACAAAATAA | TAACCAGCAG | 1800 |
| | AAAAAAGGGA | TCCAGGTGTT | ACCTGATGGT | CGGGTTACTA | ACAT T CCTCA | AGGGATGGTG | 1860 |
| 15 | ACGGACCAAT | TTGGAATGAT | TGGCCTGTTA | ACATTTATCA | GGGCAGCAGA | GACAGACCCA | 1920 |
| | GGAATGGTAC | ATCTTGCATT | AGGAAGTGAC | TTAACAACAT | TAGGCCTCAA | TCTGAACTCT | 1980 |
| 20 | CCTGAAAATC | TCTACCCCAA | ATTTGCGTCA | CCCTGGGCAT | CTTCACCTTG | TCGACCTCAA | 2040 |
| 20 | GACATAGACT | TCCATGTTCC | ATCTGAGTAC | TTAACGAACA | TTCACATTAG | GGATAAGCTG | 2100 |
| | GCTGCAATAA | AACTTGGCCG | ATATGGTGAA | GACCTTCTCT | TCTATCTCTA | TTACATGAAT | 2160 |
| 25 | GGAGGAGACG | TATTACAACT | TTTAGCTGCA | GTGGAGCTTT | TTAACCGTGA | TTGGAGATAC | 2220 |
| | CACAAAGAAG | AACGAGTATG | GATTACCAGG | GCACCAGGCA | TGGAGCCAAC | AATGAAAACC | 2280 |
| 30 | AATACCTATG | AGAGGGGAAC | ATATTACTTC | TTTGACTGTC | TTAACTGGAG | GAAAGTAGCT | 2340 |
| 50 | AAGGAGTTCC | ATCTGGAATA | TGACAAATTA | GAAGAACGGC | CTCACCTGCC | ATCCACCTTC | 2400 |
| | AACTACAACC | CTGCTCAGCA | AGCCTTCTAA | AAAAAAAA | ААААААААА | AAAAAGACTT | 2460 |
| 35 | CCCTTTTCTT | GGGGTATGGC | TGTCTCAGCA | CAATACTCAA | CATAACTGCA | GAACTGATGT | 2520 |
| | GGCTCAGGCA | CCCTGGTTTT | AATTCCTTGA | GGATCTGGCA | ATTGGCTTAC | GCAAAAGGTC | 2580 |
| 40 | ACCATTIGAG | GTCCTGCCTT | ACTAATTATG | TGCTGCCCAA | CAACTAAATT | TGTAATTTGT | 2640 |
| | TTTTCTCTAG | TTTGAGCAGG | GTCTGAATTT | TTTCATTTAT | TTCCTTTTT | GCCAGCAGAC | 2700 |
| | AGACTTGAGT | CTGTAAAGAC | AAGCAAATAC | ACTGACAGAA | GTTTACCATA | GTTTCTAAAA | 2760 |
| 45 | TGTAAAAAAG | AAAACCCCCA | AAAGACTCAA | GAAAATTAGA | CCACAAATTT | TGCATTGTTC | 2820 |
| | ATTGTAGCAC | TATTGGTAAT | AAAATAACAA | ATGTTTGTGC | ATTTTTATGT | GAAGATCCTT | 2880 |
| 50 | CTCGTATTTC | ATTTGGAAAG | ATGAGCAAGA | GGTCTGCTTC | CTTCATTTTA | CTTCCCCTTC | 2940 |
| 50 | TGTTTTTGAA | AGGCAGTTTC | GCCAAGCTTA | ATGCAAGAAT | ATCTGACTGT | TTAGAAGAAA | 3000 |
| | GATATTGCCA | CAATCTCTGG | ATGGTTTTCC | AGGGTTGTGT | ' TATTACTGAG | CTTCATCTTT | 3060 |
| 55 | CCAGAATGAG | CAAAACACTG | TCCAGTCTT | GTTACGATTI | TGTAATAAAT | GTGTACATTT | 3120 |
| | TTTTTAAATT | TTTGGACATO | ACATGAATAA | AGGTATGTAT | GTACGAATGT | GTATATATTA | 3180 |
| 60 | TATATATGAC | ATCTATTTC | GAAAATGTT | r GCCCTGCTGT | ACCTCATTT | TAGGAGGTGT | 3240 |
| | | | | | | | |

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| | GCATGGATGC AATATATGAA AATGGGACAT TCTGGAACTG CTGGTCAGGG GACTTTGTCG | 3300 |
|-----|--|------|
| | CCCTGTGCAC TAAAAGGGCC AGATTTTCAG CAGCCAAGGA CATCCATACC CAAGTGAATG | 3360 |
| 5 | TGATGGGACT TAAAAGAAGT GAACTGAGAC AATTCACTCT GGCTGTTTGA ACAGCAGCGT | 3420 |
| | TTCATAGGAA GAGAAAAAA GATCAATCTT GTATTTTCTG ACCACATAAA GGCTTCTTCT | 3480 |
| 10 | CTTTGTAATA AAGTAGAAAA GCTCTCCTCA AAAAAAAAAA | 3533 |
| 15 | (2) INFORMATION FOR SEQ ID NO: 25: (i) SEQUENCE CHARACTERISTICS: | |
| 20 | (A) LENGTH: 1148 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25: | |
| 25 | ACCCACGCGT CCGCAAATTA TACTTCCTCA TTCATATTAT GTTGATACAA AAGACCTTGG | 60 |
| 25 | CAGCCATTTC TCCCAGCAGT TITAAAGGAT GAACATTGGA TTTCATGCCA TCCCATAGAA | 120 |
| | AACCTGTTTT AAAATTTTAG GGATCTTTAC TTGGTCATAC ATGAAAAGTA CACTGCTTAG | 180 |
| 30 | AAATTATAGA CTATTATGAT CTGTCCACAG TGCCCATTGT CACTTCTTTG TCTCATTTCT | 240 |
| | TCCCTTTGTT CCTTAGTCAT CCAAATAAGC CTGAAAACCA TAAGAGATAT TACTTTATTG | 300 |
| 35 | AATATGGTTG GCATTAAATT TAGCATTTCA TTATCTAACA AAATTAATAT AAATTCCAGG | 360 |
| 33 | ACATGGTAAA ATGTGTTTTA ATAACCCCCA GACCCAAATG AAAATTTCAA AGTCAATACC | 420 |
| | AGCAGATTCA TGAAAGTAAA TTTAGTCCTA TAATTTTCAG CTTAATTATA AACAAAGGAA | 480 |
| 40 | CAAATAAGTG GAAGGGCAGC TATTACCATT CGCTTAGTCA AAACATTCGG TTACTGCCCT | 540 |
| | TTAATACACT CCTATCATCA GCACTTCCAC CATGTATTAC AAGTCTTGAC CCATCCCTGT | 600 |
| 45" | CGTAACTCCA GTAAAAGTTA CTGTTACTAG AAAATTTTTA TCAATTAACT GACAAATAGT | 660 |
| 45 | TTCTTTTTAA AGTAGTTTCT TCCATCTTTA TTCTGACTAG CTTCCAAAAT GTGTTCCCTT | 720 |
| | TTTGAATCGA GGTTTTTTTG TTTTGTTTTG TTTTCTGAAA AAATCATACA ACTTTGTGCT | 780 |
| 50 | TCTATTGCTT TTTTGTGTTT TGTTAAGCAT GTCCCTTGGC CCAAATGGAA GAGGAAATGT | 840 |
| | TTAATTAATG CTTTTTAGTT TAAATAAATT GAATCATTTA TAATAATCAG TGTTAACAAT | 900 |
| | TTAGTGACCC TTGGTAGGTT AAAGGTTGCA TTATTTATAC TTGAGATTTT TTTCCCCTAA | 960 |

CTATTCTGTT TTTTGTACTT TAAAACTATG GGGGAAATAT CACTGGTCTG TCAAGAAACA

GCAGTAATTA TTACTGAGTT AAATTGAAAA GTCCAGTGGA CCAGGCATTT CTTATATAAA

TAAAATTGGT GGTACTAATG TGAAAAAAAA AAAAAAAAA AACTCGAGGG GGGCCCGGTA

1020

1080

1140

55

PCT/US98/05311

| | CCCTATTA | 1148 |
|------------|---|------|
| 5 | | |
| | (2) INFORMATION FOR SEQ ID NO: 26: | |
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 717 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26: | |
| | GGCACGAGCT AGCTGCCGCC ACCCGAACAG CCTGTCCTGG TGCCCCGGCT CCCTGCCCCG | 60 |
| 20 | CGCCCAGTCA TGACCCTGCG CCCCTCACTC CTCCCGCTCC ATCTGCTGCT GCTGCTGCTG | 120 |
| 20 | CTCAGTGCGG CGGTGTGCCG GGCTGAGGCT GGGCTCGAAA CCGAAAGTCC CGTCCGGACC | 180 |
| | CTCCAAGTGG AGACCCTGGT GGAGCCCCCA GAACCATGTG CCGAGCCCGC TGCTTTTGGA | 240 |
| 25 | GACACGCTTC ACATACACTA CACGGGAAGC TTGGTAGATG GACGTATTAT TGACACCTCC | 300 |
| | CTGACCAGAG ACCCTCTGGT TATAGAACTT GGCCAAAAGC AGGTGATTCC AGGTCTGGAG | 360 |
| 30 | CAGAGTCTTC TCGACATGTG TGTGGGAGAG AAGCGAAGGG CAATCATTCC TTCTCACTTG | 420 |
| 30 | GCCTATGGAA AACGGGGATT TCCACCATCT GTCCCAGCGG ATGCAGTGCT GCAGTATGAC | 480 |
| | GTGGAGCTGA TTGCACTAAT CCGAGCCAAC TACTGGCTAA AGCTGGTGAA GGGCATTTTG | 540 |
| 35 | CCTCTGGTAG GGATGGCCAT GGTGCCAGCC CTCCTGGGCC TCATTGGGTA TCACCTATAC | 600 |
| | AGAAAGGCCA ATAGACCCAA AGTCTCCAAA AAGAAGCTCA AGGAAGAGAA ACGAAACAAG | 660 |
| 40 | АGCAAAAAGA ААТААТАААТ ААТАААТТТ ААААААААA ААААAAAA ААААAAA | 717 |
| 45 | (2) INFORMATION FOR SEQ ID NO: 27: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1099 base pairs | |
| 50 | (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27: | |
| 55 | GGCACGAGCC GATGTGGACA TCATCCTGTC TATCCCCATG TTCCTGCGCC TGTACCTGAT | 60 |
| - - | CGCCCGAGTC ATGCTGCTGC ACAGCAAGCT CTTCACCGAT GCCTCGTCCC GCAGCATCGG | 120 |
| | GGCCCTCAAC AAGATCAACT TCAACACCCG CTTTGTCATG AAGACGCTCA TGACCATCTG | 180 |
| 60 | CCCTGGCACT GTGCTGCTCG TGTTCAGCAT CTCTCTGTGG ATCATTGCTG CCTGGACCGT | 240 |

| | CCGTGTCTGT | GAAAGTCCTG | AATCACCAGC | CCAGCCTTCT | GGCTCATCAC | TTCCTGCTTG | 300 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | GTACCATGAC | CAGCAGGACG | TAACTAGTAA | CTTTCTGGGT | GCCATGTGGC | TCATCTCCAT | 360 |
| 3 | CACATTCCTT | TCCATTGGTT | ATGGGGACAT | GGTGCCCCAC | ACATACTGTG | GGAAAGGTGT | 420 |
| | CTGTCTCCTC | ACTGGCATCA | TGGGTGCAGG | CTGCACTGCC | CTTGTGGTGG | CCGTGGTGGC | 480 |
| 10 | CCGAAAGCTG | GAACTCACCA | AAGCGGAGAA | GCACGTTCAT | AACTTCATGA | TGGACACTCA | 540 |
| | GCTCACCAAG | CGGATCAAGA | ATGCTGCAGC | CAATGTCCTT | CGGGAAACAT | GGTTAATCTA | 600 |
| 15 | TAAACACACA | AAGCTGCTAA | AGAAGATTGA | CCATGCCAAA | GTGAGGAAAC | ACCAGAGGAA | 660 |
| 15 | GTTCCTCCCA | AGCTATCCAC | CAGTTTGAGG | AGCGTCCCAG | ATGGAACAGA | GGAAAGCTGA | 720 |
| | GTGACCAAGC | CAACACTCTG | GTGGACCTTT | CCAAGATGCA | GAATGTCATG | TATGACTTAA | 780 |
| 20 | TCACAGAACT | CAATGACCGG | AGCGAAGACC | TGGAGAAGCA | GATTGGCAGC | CTGGAGTCGA | 840 |
| | AGCTGGAGCA | TCTCACCGCC | AGCTTCAACT | CCCTGCCGCT | GCTCATCGCC | GACACCCTGC | 900 |
| 25 | GCCAGCAGCA | GCAGCAGCTC | CTGTCTGCCA | TCATCGAGGC | CCGGGGTGTC | AGCGTGGCAG | 960 |
| 23 | TGGGCACCAC | CCACACCCCA | ATCTCCGATA | GCCCCATTGG | GGTCAGCTCC | ACCTCCTTCC | 1020 |
| | CGACCCCGTN | CACAAGTTCA | AGCAGTTGCT | AAATAAATCT | CCCCACTCCA | GAAGCATTAA | 1080 |
| 30 | ААААААААА | AAAAAAAA | | | | | 1099 |

35 (2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 941 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

| 45 | AATTCGGCAG | AGAGCCAACC | GAGGGCGTTC | CTGTCGGGGC | TGCAGCGGCG | GGAGGGAGCC | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| | CAGTGGAGGC | GCCCTCCCGA | AGCGCCACTG | CCCATGCTGA | CCACCCAGCC | CTCCGGCTGC | 120 |
| 50 | TGATGTCATG | AGTAACACCA | CTGTGCCCAA | TGCCCCCCAG | GCCAACAGCG | ACTCCATGGT | 180 |
| 30 | GGGCTATGTG | TTGGGGCCCT | TCTTCCTCAT | CACCCTGGTC | GGGGTGGTGG | TGGCTGTGGT | 240 |
| | AATGTATGTA | CAGAAGAAAA | AGCGGGTGGA | CCGGCTGCGC | CATCACCTGC | TCCCCATGTA | 300 |
| 55 | CAGCTATGAC | CCAGCTGAGG | AACTGCATGA | GGCTGAGCAG | GAGCTGCTCT | CTGACATGGG | 360 |
| | AGACCCCAAG | GTGGTACATG | GCTGGCAGAG | TGGCTACCAG | CACAAGCGGA | TGCCACTGCT | 420 |
| 60 | GGATGTCAAG | ACGTGACCTG | ACCCCCTTGC | CCCACCCTTC | AGAGCCTGGG | GTYCTGGACT | 480 |

| | GCCTGGGGCC | CTGCCATCTG | CTTCCCCTGC | TGTCACCTGG | STCCCCCTGC | TGGGTGCTGG | 540 |
|----|------------|------------|------------|------------|------------|------------|-------------|
| | GTCTCCATTT | CTCCCTCCAC | CCACCCTCAG | CAGCATCTGC | TTCCCATGCC | CTCACCATCA | 600 |
| 5 | CCTCACTGCC | CCCAGGCCTT | CTGCCCTTTG | TGGGTGTTGA | GCTCACCGCC | CACCCACAGG | 660 |
| | CACTCATGGG | AAGAGGCTTT | CCTTCTGGGA | TGGCGGCGGC | TGGTAGACAC | CTTTGCTTTC | 7 20 |
| 10 | TCTAGCCCTC | CTGGGCTGGG | CTTGGGCACA | AATCCCCAGG | CAGGCTTTGG | AGTTGTTTCC | 780 |
| ıU | ATGGTGATGG | GGCCAGATGT | ATAGTATTCA | GTATATATTT | TGTAAATAAA | ATGTTTIGTG | 840 |
| | GCTAAAAAAA | АААААААА | ATCNAAGGG | GGGCCGGTAC | CCAAATTCCC | CCTATANTGA | 900 |
| 15 | ATTCGTATTA | ACAATTCACT | TGGGGCCGTC | CTTTTAANAA | С | | 941 |
| | | | | | | | |

20 (2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 756 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

| 30 | GGCACGAGGA | AGCTGGAGCG | GCCGGCGT | GCAGTCACGG | GGGAGCGAGG | CCTGCTGGGC | 60 |
|----|------------|------------|------------|------------|------------|------------|-------------|
| | TTGGCAACGA | GGGACTCGGC | CTCGGAGGCG | ACCCAGACCA | CACAGACACT | GGGTCAAGGA | 120 |
| 35 | GTAAGCAGAG | GATAAACAAC | TGGAAGGAGA | GCAAGCACAA | AGTCATCATG | GCTTCAGCGT | 180 |
| | CTGCTCGTGG | AAACCAAGAT | AAAGATGCCC | ATTITCCACC | ACCAAGCAAG | CAGAGCCTGT | 240 |
| | TGTTTTGTCC | AAAATCAAAA | CTGCACATCC | ACAGAGCAGA | GATCTCAAAG | ATTATGCGAG | 300 |
| 40 | AATGTCAGGA | AGAAAGTTTC | TGGAAGAGAG | CTCTGCCTTT | TTCTCTTGTA | AGCATGCTTG | 360 |
| | TCACCCAGGG | ACTAGTCTAC | CAAGGTTATT | TGGCAGCTAA | TTCTAGATTT | GGATCATTGC | 420 |
| 45 | CCAAAGTTGC | ACTTGCTGGT | CTCTTGGGAT | TTGGCCTTGG | AAAGGTATCA | TACATAGGAG | 480 |
| 43 | TATGCCAGAG | TAAATTCCAT | TTTTTTGAAG | ATCAGCTCCG | TGGGGCTGGT | TTTGGTCCAC | 540 |
| | AGCATAACAG | GCACTGCCTC | CTTACCTGTG | AGGAATGCAA | AATAAAGCAT | GGATTAAGTG | 600 |
| 50 | AGAAGGGAGA | CTCTCAGCCT | TCAGCTTCCT | AAATTCTGTG | TCTGTGACTT | TCGAAGTTTT | 660 |
| | TTAAACCTCT | GAATTTGTAC | ACATTTAAAA | TTTCAAGTGT | ACTTTAAAAT | AAAATACTTC | 720 |
| 55 | TAATGGAAAA | ААААААААА | AAAAAAAA | ACTCGA | | | 7 56 |

(2) INFORMATION FOR SEQ ID NO: 30:

60

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2100 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

| 10 | NCCAGAGGCA | GAAAGTCCTG | CTTCTGGGGC | GTAACCTACA | GGATATCCTT | GGAACAGAAG | 60 |
|-----|------------|------------|---|------------|------------|------------|------|
| 10 | ATCTTATTGT | GGAAGTRACT | TCCAATGATG | CTGTGAGATT | TTATCCCTGG | ACCATTGATA | 120 |
| | АТАААТАСТА | TTCAGCAGAC | ATCAATCTAT | GTGTGGTGCC | AAACAAATTT | CTTGTTACTG | 180 |
| 15. | CAGAGATTGC | AGAATCTGTC | CAAGCATTTG | TGGTTTACTT | TGACAGCACA | CAAAAATCGG | 240 |
| | GCCTTGATAG | TGTCTCCTCA | TGGCTTCCAC | TGGCAAAAGC | ATGGTTACCY | GAGGTGATGA | 300 |
| 20 | TCTTGGTCTG | CGATAGAGTG | TCTGAAGATG | GTATAAACCG | ACAAAAAGCT | CAAGAATGGT | 360 |
| 20 | GCATCCAAAC | ATGGCTTTGA | ATTGGTAGAA | CTTAGTCCAG | AGGAGTTGCC | TGAGGAGGAT | 420 |
| | GATGACTTCC | CAGAATCTAC | AGGAGTAAAG | CGAATTGTCC | AAGCCCTGAA | TGCCAATGTG | 480 |
| 25 | TGGTCCAATG | TAGTGATGAA | GAATGATAGG | AACCAAGGCT | TTAGCTTGCT | GCAACTCATT | 540 |
| | GACTGGAACA | AACCATAGCA | TTGGGTCAGC | AGATCCCTGT | CACCCAGAGC | AACCCCATTT | 600 |
| 30 | GCCAGCAGCA | GATAGTACTG | AATCCCTCTC | TGATCATCGG | GGTGGTGCAT | CTAACACAAC | 660 |
| 30 | AGATGCCCAG | GTTGATAGCA | TTGTGGATCC | CATGTTAGAT | CTGGATATTC | AAGAATTAGC | 720 |
| | CAGTCTTACC | ACTGGAGGAG | GAGATGTGGA | GAATTTTGAA | AGACTCTTTT | CAAAGTTAAA | 780 |
| 35 | GCAAATGAAA | GACAAGGCTG | CGACGCTTCC | TCATGAGCAA | AGAAAAGTGC | ATGCAGAAAA | 840 |
| | GGTGGCCAAA | GCATTCTGGA | TGGCAATCGG | GGGAGACAGA | GATGAAATTG | AAGGCCTTTC | 900 |
| 40 | ATCTGATGAA | GAGCACTGAA | TTATTCATAC | TAGGGTTTGA | CCAACAAAGA | TGCTAGCTGT | 960 |
| 10 | CTCTGAGATA | CCTCTCTACT | CAGCCCAGTC | ATATTTTGCC | AAAATTGCCC | TTATCATGTT | 1020 |
| | GGCTGCCTGA | CTTGTTTATA | GGGTCCCCTT | AATTTTAGTT | TTTAGTAGGA | GGTTAAGGAG | 1080 |
| 45 | AAATCTTTTT | TTTCCTCAGT | ATATTGTAAG | AGAGTGAGGA | ATACAGTGAT | AGTAATGAGT | 1140 |
| | GAGGATTTCT | TAAATRTACT | TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT | TCTAGGAATG | AGGGTAGGAT | AAATCTCAGA | 1200 |
| 50 | GGTCTGTGTG | ATTTACTCAA | GTTGAAGACA | ACCTCCAGGC | CATTCCTGGT | CAACCTTTTA | 1260 |
| 30 | AGTAGCATTT | CCAGCATTCA | CACTTGATAC | TGCACATCAG | GAGTTGTGTC | ACCTTTCCTG | 1320 |
| | GGTGATTTGG | GTTTTCTCCA | TTCAAGGAGC | TTGTAGCTCT | GAAGCTATGA | TGCTTTTATT | 1380 |
| 55 | GGGAGGAAAG | GAGGCAGCTG | CAGAATTGAT | GTGAGCTATG | TGGGGCCGAA | GTCTCAGCCC | 1440 |
| | GCAGCTAAGT | CTCTACCTAA | GAAAATGCCT | CTGGGCATTC | TTTTGAAGTA | TAGTGTCTGA | 1500 |
| 60 | GCTCATGCTA | GAAAGAATCA | AAAAGCCAGT | GTGGATTTTT | AGACTGTAAT | AAATGAGGCA | 1560 |

| | AAGGATTTCT | ATTCCAGTGG | GAAGRAAACC | TCTCTACTGA | GTTGTGGGG | ATATGTTGTA | 1620 |
|----|--------------|------------|------------|------------|------------|------------|------|
| | TGTTAGAGAG | AACCTTAAGG | AGTCCTTGTA | TGGGCCATGG | AGACAGTATG | TGATAACATA | 1680 |
| 5 | . CCGTGATTTT | CATGAAGAAA | TTCTTCTGTC | TTAGAGTTCT | CCCCTGCTGC | TTGAGATGCC | 1740 |
| | AGAGCTGTGT | TGTTGCACAC | CTGCAAAACA | AGGCACATTT | CCCCCTTTCT | CTTTAAAGCC | 1800 |
| 10 | AAAGAGAGAT | CACTGCCAAA | GTGGGAGCAC | TAAGGGGTGG | GTGGGGAAGT | GAAATGTTAG | 1860 |
| | GCGATGAATT | CCTGAGCACC | TIGTTTTTCT | TCCAAGGTTC | GTAGCTCCTC | TCTGCCCTTC | 1920 |
| | CAAGCCTGTA | ACCTCGGAGG | ACTATCTTTT | GTTCTTTATC | CTTTGTCTTG | TTTGAGTGGG | 1980 |
| 15 | TCAGCCCCAG | AGGAACTGAT | AAGCAAATGG | CAAGTTTTTA | AAGGAAGAGT | GGAAAGTACT | 2040 |
| | GCAAATAAAA | ATCCTTATTT | GTTTTTGTAG | AAAAAAAA | AAAAAAAA | AAAAAAAAAG | 2100 |

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(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1448 base pairs

(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

| | AAAAAAAAA | AAAGCCCACC | TGAAAGCCTG | TCTCTTTCCA | CTTTGTTGGC | CCTTCCAGTG | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 35 | GGATTATCGA | GCATGTTGTT | TTTTCATAGT | GCCTTTTTCC | TTATTTCAAG | GGTTGCTTCT | 120 |
| 33 | GAGTGGTGTT | TTTTTTTT | TTAATTIGTT | TTGTTTTAAA | ATAAGTTAAA | GACAGTCCAG | 180 |
| | AGCTTTTCAG | CCAATTTGTC | TCCTACTCTG | TGTAAATATT | TTTCCCTCCG | GGCAGGGGAG | 240 |
| 40 | CCAGGGTAGA | GCAAAGGAGA | CAAGCAGGAG | TGGAAGGTGA | GGCGTTCTCC | TGCTTGTACT | 300 |
| | AAGCCAGGAG | STTTAAGCTC | CAGCTTTAAG | GGTTGTGAGC | CCCTTGGGGT | TCAGGGAACT | 360 |
| 45 | GCTTGCCCAG | GGTGCAGTGT | GAGTGTGATG | GGCCACCGGG | GCAAGAGGGA | AGGTGACCGC | 420 |
| 45 | CCAGCTCTCC | CACATCCCAC | TGGATCTGGC | TTACAGGGG | GTCGGAAGCC | TGTCCTCACC | 480 |
| | GTCTCGGGGG | TTGTGGCCCC | CGCCCCCTCC | CTATATGCAC | CCCTGGAACC | AGCAAGTCCC | 540 |
| 50 | AGACAAGGAG | AGCGGAGGAG | GAAGTCATGG | GAACGCAGCC | TCCAGTTGTA | GCAGGTTTCA | 600 |
| | CTATTCCTAT | GCTGGGGTAC | ACAGTGAGAG | TACTCACTTT | TCACTTGTCT | TGCTCTTAGA | 660 |
| 55 | TTGGGCCATG | GCTTTCATCC | TGTGTCCCCT | GACCTGTCCA | GGTGAGTGTG | AGGGCAGCAC | 720 |
| 33 | TGGGAAGCTG | GAGTGCTGCT | TGTGCCTCCC | TTCCCAGTGG | GCTGTGTTGA | CTGCTGCTCC | 780 |
| | CCACCCTAC | CGATGGTCCC | AGGAAGCAGG | GAGAGTTGGG | GAAGGCAAGA | TTGGAAAGAC | 840 |
| 60 | AGGAAGACCA | AGGCCTCGGC | AGAACTCTCT | GTCTTCTCTC | CACTTCTGGT | CCCCTGTGGT | 900 |

| | GATGTGCCTG TAATCTTTTT CTCCACCCAA ACCCCTTCCC ACGACAAAAA CAAGACTGCC | 960 |
|-----|---|------|
| 5 | TCCCTCTCTT CCGGGAGCTG GTGACAGCCT TGGGCCTTTC AGTCCCAAAG CGGCCGATGG | 1020 |
| 3 | GAGTCTCCCT CCGACTCCAG ATATGAACAG GGCCCAGGCC TGGAGCGTTT GCTGTGCCAG | 1080 |
| | GAGGCGGCAG CTCTTCTGGG CAGAGCCTGT CCCCGCCTTC CCTCACTCTT CCTCATCCTG | 1140 |
| 10 | CTTCTCTTTT CCTCGCAGAT GATAAAAGGA ATCTGGCATT CTACACCTGG ACCATTTGAT | 1200 |
| | TGTTTTATTT TGGAATTGGT GTATATCATG AAGCCTTGCT GAACTAAGTT TTGTGTGTAT | 1260 |
| 1.5 | ATATTTAAAA AAAAAATCAG TGTTTAAATA AAGACCTATG TACTTAATCC TTTAACTCTG | 1320 |
| 15 | CGGATAGCAT TTGGTAGGTA GTGATTAACT GTGAATAATA AATACACAAT GAATTCTTMA | 1380 |
| | AAAAAAAAA AAAAAAAAA AAAAAAAAAA AAACCCCGGG GGGGGCCCCG GGCCCCAATT | 1440 |
| 20 | CCCCCCAA | 1448 |
| | | |
| 25 | (a) THEODY MICH FOR STO ID NO. 22 | |
| 25 | (2) INFORMATION FOR SEQ ID NO: 32: | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 456 base pairs | |
| 30 | (B) TYPE: nucleic acid (C) STRANDEDNESS: double | |
| | (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32: | |
| 35 | GGCACAGCAA ACTTGACGCC ATGAAGATCC CGGTCCTTCC TGCCGTGGTG CTCCTCTCCC | 60 |
| | TCCTGGTGCT CCACTCTGCC CAGGGAGCCA CCCTGGGTGG TCCTGAGGAA GAAAGCACCA | 120 |
| 40 | TTGAGAATTA TGCGTCACGA CCCGAGGCCT TTAACACCCC GTTCCTGAAC ATCGACAAAT | 180 |
| 70 | TGCGATCTGC GTTTAAGGCT GATGAGTTCC TGAACTGGCA CGCCCTCTTT GAGTCTATCA | 240 |
| | AAAGGAAACT TCCTTTCCTC AACTGGGATG CCTTTCCTAA GCTGAAAGGA CTGAGGAGCG | 300 |
| 45 | CAACTCCTGA TGCCCAGTGA CCATGACCTC CACTGGAAGA GGGGGCTAGC GTGAGCGCTG | 360 |
| | ATTCTCAACC TACCATAACT CTTTCCTGCC TCAGGAACTC CAATAAAACA TTTTCCATCC | 420 |
| 50 | AAAAAAAAA AAAAAAAAAC CCCNGGGGGG GCCCGG | 456 |
| 30 | | |
| | | |
| 55 | (2) INFORMATION FOR SEQ ID NO: 33: | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1326 base pairs | |

(B) TYPE: nucleic acid(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

| (xi) S | SEQUENCE | DESCRIPTION: | SEQ | ID | NO: | 33: |
|--------|----------|--------------|-----|----|-----|-----|
|--------|----------|--------------|-----|----|-----|-----|

| 5 | GGCACGAGTG | CAGGCCCAGA | GAGGACTCAT | TGAAAGGACT | GAAAGGGGAG | GTGGCGTTTT | 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| 3 | CTTCCTACCC | AAACTTACCC | CTGTGAGCTG | GACAGCTTGG | TAGCACCTGC | CTGGACTTAG | 120 |
| | ATGGTGGTAG | CCAAGAAGAC | TGACATTTTA | GGGAACAGGA | CGGGGAGGAG | AAGGCTCTGG | 180 |
| 10 | CACACACACA | TGTGTCCATA | TGTCCTGCAA | TGGTCTGGGG | ACTATTGCTA | GGCTAGGAGC | 240 |
| | CCTAAGTGTC | TTCTTCCTCA | TGTCTMTTCT | CCCCTGTSTC | ATGGGCCCTA | AGRTCTCTTT | 300 |
| 15 | CACTGGGCCT | GCCTCAATGA | ACGTGCTGCC | CAGCTACCCC | GAAACACGGC | ANCTGCCGGC | 360 |
| 13 | TATCAATGCC | CCAGCTGCAA | TGGCCCATCT | TCCCCCAACC | AACCTGGCTG | GCCCGTGGG | 420 |
| | CTCCGCACTG | AGARARAAAS | TTGGCACART | CAACTGGGCC | CGGGCAGGAC | TGGGCCYCCC | 480 |
| 20 | TCTGATCGAT | GAAGKTGGTG | ARCCCAGAGC | CCGAGCCCCT | CAACACGTCT | GACTTCTCTG | 540 |
| | ACTGGTCTAG | TTTTAATGCC | AGCAGTACCC | CTGGACCAGA | GGAGGTAGAC | AGCGCCTCTG | 600 |
| 25 | CTGCCCCAGC | CTTCTACAGC | CGAGCCCCCC | GGCCCCCAGC | TTCCCCAGGC | CGGCCCGAGC | 660 |
| 23 | AGCACACAGT | GATCCACATG | GGCAATCCTG | AGCCCTTGAC | TCACGCCCCT | AGGAAGGTGT | 720 |
| | ATGATACGCG | GGATGATGAC | CGGACACCAG | GCCTCCATGG | AGACTGTGAC | GATGACAAGT | 780 |
| 30 | ACCGACGTCG | GCCGGCCTTG | GGTTGGCTGG | CCCGGCTGCT | AAGGAGCCGG | GCTGGGTCTC | 840 |
| | GGAAGCGRCC | GCTGACCCTG | CTCCAGCGGG | CGGGGCTGCT | GCTACTCTTG | GGACTGCTGG | 900 |
| 35 | GCTTCCTGGC | CCTCCTTGCC | CTCATGTCTC | GCCTAGGCCG | GGCCGCAGCT | GACAGCGATC | 960 |
| 33 | CCAACCTGGA | CCCACTCATG | AACCCTCACA | TCCGCGTGGG | CCCCTCCTGA | GCCCCCTTGC | 1020 |
| | TTGTGGCTAG | GCCAGCCTAG | GATGTGGGTT | CTGTGGAGGA | GAGGCGGGT | AATGGGGAGG | 1080 |
| 40 | CTGAGGGCAC | CTCTTCACTG | CCCCTCTCCC | TCAAGCCTAA | GACACTAAGA | CCCCAGACCC | 1140 |
| | AAAGCCAAGT | CCACCAGAGT | GGCTGCAGGC | CAGGCCTGGA | GTCCCCGTGG | GTCAAGCATT | 1200 |
| 45 | TGTCTTGACT | TGCTTTCCTC | CCGGGTYTCC | AGCCTCCGAC | CCCTCGCCCC | ATGAAGGAGC | 126 |
| 13 | TGGCAGGTGG | AAATAAACAA | CAACTITATT | AAAAAAAA | ААААААААА | AAAAAAAAA | 1320 |
| | AANAA | | | | | | 132 |

(2) INFORMATION FOR SEQ ID NO: 34:

55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 710 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

190

| | (xi) | SEQUENCE D | ESCRIPTION: | SEQ ID NO | : 34: | | |
|----|--------------|--------------|-----------------------------|------------|------------|------------|-----|
| | GCGAAAGAGA | AAAAGGCTGG | AGCTCCCGCC | CCCGGGGCTG | TCAGATGGCT | TGGGTTTCTG | 60 |
| 5 | CGACGCGATT | GGCTCGCGGA (| GGCAGAAAT | TACTCAGCAA | ACATGACTAT | TATTAGCTGC | 120 |
| | TTAGCAACAG | CTCACCAAAG | TAGAGAGACC | ACCCAGGTAG | GCAACCCAGT | GTGTGCATCC | 180 |
| 10 | TCGGCTTCGG | GGCAGCCTCT (| GAGAGCGCCA | ACCTTCTCGC | ATGCAATACT | TCCATTAAGG | 240 |
| 10 | AATGCTCCCC | CTCCTTTCTC ' | TCTTATTCCT | TTTCTTTTCA | ACAGTGTCTT | CTTTTTGTGG | 300 |
| | GATGCCTTTG | CGCGCACACA (| CGCGCGCGCA | SGCACACACA | CGAACATTTG | CCTCGCGGTA | 360 |
| 15 | GACACGGGGG | GAAATGTWAT A | ATTTTTTAA | GCGCTTAAAC | AATTTCTGAA | ATTCCTCAAA | 420 |
| | GAAAAGCCTT ' | TCAGARGCAC (| CTTGGCCTCA | AGCTGCAACA | AATACTGGGA | RGTCCGGCTC | 480 |
| 20 | GCATTCCCAG | GCCTGCACCA | ATAATGACAG | CGTGCTGGAT | ARTGCGCCAG | TGTGTGCCAG | 540 |
| 20 | ATTTTTTTT | CCTCTTCTCT ' | TTTCTTTTAT | AACTAAAGGG | AAGACTTAGG | CTCTTGCAGG | 600 |
| | GAACAACGCC | TCGCATTAAG | ATAAACAGAA | TGGAAAGTTA | AAGAGGAAAG | CAAGGACGTT | 660 |
| 25 | GGGAAAAGCC . | ATCTTTCTTA | AAATCCGTCT | GCCCCCAGC | CGCTTTCTCC | | 710 |
| | | | | | | | |
| 20 | | | o TD NO 35 | | | | |
| 30 | (2) INFORMA | | - | | | | |
| | (1) | | TH: 1188 b | ase pairs | | | |
| 35 | | (C) STRA | E: nucleic a NDEDNESS: a | double | | | |
| | , | | COGY: line | | 25 | | |
| 40 | | SEQUENCE D | | _ | | | 50 |
| 40 | GATGGCTTTT | | | | | | 60 |
| | GATATGGTGG | | | | | | 120 |
| 45 | TACGACATTA | | | | | | 180 |
| | ATCTGTGAGA | | | | | | 240 |
| | CTGGCCCCAC | CACAGCCGCC | CCTTCCTGAA | ACCATAGAGC | GGCCGGTGGG | CACTGGGGCC | 300 |
| 50 | ATGGTGGCTC | | | | | | 360 |
| | GTTCTCATCA | TCGTCACCTT | CATCCCCTTC | TGCTTGTGGA | GGCCTGGTC | TAAGCAAAAA | 420 |
| | CATACAACAG | ACCTGGGTTT | TCCTCGAAGT | GCCCTTCCAC | CCTCCTGCCC | GTATACTATG | 480 |

GTGCCATTGG GAGGACTCCC AGGCCACCAG GCAGTGGACA GCCCTACCTC AGTGGCATCA

GTGGACGGC CTGTGCTAAT GGGATCCACA TGAATAGGGG CTGCCCCTCG GCTGCAGTGG

GCTACCCGGG CATGAAGCCC CAGCAGCACT GCCCAGGCGA GCTTCAGCAG CAGAGTGACA

540

600

660

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| CCAGCAGCCT | GCTGAGGCAG | ACCCATCTTG | GCAATGGATA | TGACCCCCAA | AGTCACCAGA | 720 |
|------------|--|---|--|--|--|--|
| TCACGAGGGG | TCCCAAGTCT | AGCCCGGACG | AGGGCTCTTT | CTTATACACA | CTGCCCGACG | 780 |
| ACTCCACTCA | CCAGCTGCTG | CAGCCCCATC | ACGACTGCTG | CCAACGCCAG | GAGCAGCCTG | 840 |
| CTGSTGTGGG | CCAGTCAGGG | GTGAGGAGAG | CCCCGACAG | TCCTGTCCTG | GAAGCAGTGT | 900 |
| GGGACCCTCC | ATTTCACTCA | GGGCCCCCAT | GCTGCTTGGG | CCTTGTGCCA | GTTGAAGAGG | 960 |
| TGGACAGTCC | TGACTCCTGC | CAAGTGAGTG | GAGGAGACTG | GTGTCCCCAG | CACCCCGTAG | 1020 |
| GGGCCTACGT | AGGACAGGAA | CCTGGAATGC | AGCTCTCCCC | GGGCCACTG | GTGCGTGTGT | 1080 |
| CTTTTGAAAC | ACCACCTCTC | ACAATTTAGG | CAGAAGCTGA | TATCCCAGAA | AGACTATATA | 1140 |
| TTGTTTTTT | TTTAAAAAAA | АААААААА | AWCYCGGGGG | GGGGCCCC | | 1188 |
| | TCACGAGGGG ACTCCACTCA CTGSTGTGGG GGGACCCTCC TGGACAGTCC GGGCCTACGT CTTTTGAAAC | TCACGAGGGG TCCCAAGTCT ACTCCACTCA CCAGCTGCTG CTGSTGTGGG CCAGTCAGGG GGGACCCTCC ATTTCACTCA TGGACAGTCC TGACTCCTGC GGGCCTACGT AGGACAGGAA CTTTTGAAAC ACCACCTCTC | TCACGAGGGG TCCCAAGTCT AGCCCGGACG ACTCCACTCA CCAGCTGCTG CAGCCCCATC CTGSTGTGGG CCAGTCAGGG GTGAGGAGAG GGGACCCTCC ATTTCACTCA GGGCCCCCAT TGGACAGTCC TGACTCCTGC CAAGTGAGTG GGGCCTACGT AGGACAGGAA CCTGGAATGC CTTTTGAAAC ACCACCTCTC ACAATTTAGG | TCACGAGGG TCCCAAGTCT AGCCCGGACG AGGGCTCTTT ACTCCACTCA CCAGCTGCTG CAGCCCCATC ACGACTGCTG CTGSTGTGGG CCAGTCAGGG GTGAGGAGAG CCCCCGACAG GGGACCCTCC ATTTCACTCA GGGCCCCCAT GCTGCTTGGG TGGACAGTCC TGACTCCTGC CAAGTGAGTG GAGGAGACTG GGGCCTACGT AGGACAGGAA CCTGGAATGC AGCTCTCCCC CTTTTGAAAC ACCACCTCTC ACAATTTAGG CAGAAGCTGA | TCACGAGGGG TCCCAAGTCT AGCCCGGACG AGGGCTCTTT CTTATACACA ACTCCACTCA CCAGCTGCTG CAGCCCCATC ACGACTGCTG CCAACGCCAG CTGSTGTGGG CCAGTCAGGG GTGAGGAGAG CCCCCGACAG TCCTGTCCTG | CCAGCAGCCT GCTGAGGCAG ACCCATCTTG GCAATGGATA TGACCCCCAA AGTCACCAGA TCACGAGGGG TCCCAAGTCT AGCCCGGACG AGGCCTCTTT CTTATACACA CTGCCCGACG ACTCCACTCA CCAGCTGCTG CAGCCCCATC ACGACTGCTG CCAACGCCAG GAGCAGCCTG CTGSTGTGGG CCAGTCAGGG GTGAGGAGAG CCCCCGACAG TCCTGTCCTG |

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(2) INFORMATION FOR SEQ ID NO: 36:

25 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 956 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

| | GGCAGAGCAG | TGAAAATGCA | TCCTAAAAAT | TCAATGTTTA | TACCAGGCTC | ATGACACTAA | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 35 | GATGTGACAT | CTGGACACGA | GGGTCAGCC | ACGTGGATAC | ATCCCTCCCA | GATTGCATCT | 120 |
| | CCAGGAATCA | CTCTGCTAGC | AGAATGGCCG | CCCCATCCCT | TACTATGCTG | CTCCTCCTCA | 180 |
| 40 | AAGTGCAGCC | CAGAAGGACC | CAGGCCTTTG | ATGCACATTG | GGTGGGTCTC | CCACTACTTT | 240 |
| 40 | AGTTGAAATG | GGAGCATGCT | GGAGTCGGCG | TTCTGTTGCT | TCTGGTGAGA | AGGACATCCC | 300 |
| | ATTGACCCCT | GGCCACCAGG | TCCAGTATTC | CATCCTTCCT | TCTGTCCCAG | CCTATCGCCC | 360 |
| 45 | TCCCCACYAG | GCCCACCCCC | ACAACTTCTC | CTCAAGGGAG | GTTNTCCCGC | AGCTGGAGGG | 420 |
| | CTTGCACAGA | CCAGCAGTCA | CAGAAATCAT | TCTTCCTGCT | GTACTGGGCC | TTAACTGCCT | 480 |
| 50 | GCAAATGTCC | GAGCACTACT | GCATAGGATG | CCAGAGCCAC | CGAAGATAAA | CACAGCCAAG | 540 |
| 50 | тттаатаата | ATAAAAGGAA | AAATCTCAGC | CTGCAGAACT | CTGGTTTTGA | CCCACCATCG | 600 |
| | GCCAGATGCA | CATCTTCAGG | GCCTGTTGAG | CACCTTCTGA | AAAGCAGGGC | TCGTAATAGA | 660 |
| 55 | CTCCAGCACA | TTCCATCAGA | GTCAGGAAAA | CTGCGGTGAG | TCCCAGAGAA | TCTAGGGTGC | 720 |
| | AGGGCAGGGA | GCAGGAGTCA | TAAGGAGTGA | TAACCTAAAC | TGTGTGTAGT | CAGCGGGGAG | 780 |
| 60 | GGTCTTATGT | TATCAGGTGA | AATGAGAGCC | AGTAAGTTAG | TTGATCCTGT | CACAGATATA | 840 |

192

ACCCTGATAA CACCCCATAG ATACGCGACA CGTGTGTCCT GCCCCTGCTT TCCCCATCCA 900

ACATGGTTCT TCTGTTCCAC AGACATTAAA GGGGCTTTCT GCAATTACTT AAAAAA 956

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(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1603 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

TCGACCCACG CGTCCGCTCT GCCAGGAATC TGGTCTTTCT GTAGACCCAA GTCAGAAAGA 60 ACCATTTGTG GAGTTAAATC GAATATTAGA RGCATTAAAR GTCAGAGTTC TGAGACCTGC 120 TCTGGAATGG GCAGTTTCAA ACCGAGAGAT GCTTATAGCC CAAAACAGCT CCTTGGAATT 180 TAAACTACAC AGACTGTATT TTATTAGCTT RTTAATGGGT GGAACACAAA TCAGCGAGAR 240 GCATTACAAT ATGCTAAAAA TTTTCAGCCA TTTGCCCTAA ATCATCAAAA AGACATTCAG 300 GTTTTGATGG GAAGCCTTGT GTACCTGAGA CAAGGGATTG AGAACTCACC ATATGTTCAC 360 CTACTTGATG CAAACCAGTG GGCTGATATC TGTGACATCT TTACACGGGA TGCTTGTGCC 420 CTCCTGGGGC TCTCCGTGGA GTCCCCTCTC AGTGTCAGTT TCTCAGCAGG TTGTGTGGCG 480 CTGCCAGCTT TAATTAACAT CAAAGCCGTG ATTGAACAGA GGCAGTGTAC TGGAGTTTGG 540 AACCAGAAG ATGAATTACC TATTGAAGTG GACCTTGGTA AAAAGTGCTG GTATCACTCT 600 ATATTTGCCT GCCCCATTCT TCGTCAGCAA ACAACAGATA ACAATCCACC CATGAAATTG 660 GTCTGTGGTC ATATTATATC AAGAGATGCC CTGAATAAAA TGTTTAATGG TAGCAAATTA 720 AAATGTCCCT ACTGTCCAAT GGAACAAGT CCAGGAGATG CCAAACAGAT ATTTTTCTGA 780 AGAGATAACT TTAGTTTGCA ATTTGTAAGT GAAACTGAAT CGTGGGTGCA TTTCAGAAGA 840 GAACGTTCCA TATAATGCAG CTAACCAAGG ACTCCTGTGT TTCTATAAGC TAATGCTCCA 900 GAAACTITGC CAACCTGTTA GTGTACACAC ACTGAGGGGA GTGCTCCCGG TGAATATTAT 960 CATAGGETT TATTATATTC TTGGTCTTCA TTTCTGATCA AGTAAATACA CCAGCAGTTG 1020 TCATTCAATG CAGGTTTTTG TACTTAATTA TATGGTGATT TTTTTACTTT TTAAGAGCAG 1080 AAACGGAAAT TGACCTCCCC GCCATGTGTT TAATATTCCT CCTGCTTTTA CTTTTGTCAT 1140 TTTCTTGATA ATCGTAAGCC TTGAGAGTGT TTGTGAAAAA GTTTTATTTC CTGTTATGTA 1200 TACATAATTA AATGAAAATT CTTCAGAAAA AGTTTGATAA ATTGAATTGT GGTTATGAAA 1260 CTAATTIGCA TITTIATTIG CITAAGAAG AAAGCTGTGA TAGATTCCAG ATATGCTTTT 1320

| | TGATGTTTTC | CTCTGCTCCA | GCTCCAAGAA | GTCAGCACAC | CTGCATTTTA | GCTCTGCATG | 1380 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | CAGCCCCAGC | AGGCTGCGTG | TTTAAGAATT | TCATTGTTTA | ACTGGCTGGT | GTGAGAAGTC | 1440 |
| 3 | TTCCGTTAGC | ATAGAGTGGA | AGGAGTACTA | TTGTTTGGTT | GGGTTTTTGT | TTGTTTGTTT | 1500 |
| | TTTGTTTTTG | CTTTTATTGC | CAAGAGGTGC | TTGTTTTAAA | AGTATGTTTA | ATAAAATGAA | 1560 |
| 10 | ATTCTAAAGT | TAARAAGTGT | TCTTAAAGTT | GATATTTAAC | TCT | | 1603 |

15 (2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1089 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

| 25 | GGCACGAGCT | ACCTTTCTGC | CTGCTTTGCT | GGCTGCAACA | GCACGAATCT | CACGGGCTGT | 60 |
|----|------------|------------|------------|--------------|--------------|------------|------|
| | GCGTGCCTCA | CCACCGTCCC | TGCTGAGAAC | GCAACCGTGG | TTCCTGGAAA | ATGCCCCAGT | 120 |
| 30 | CCTGGGTGCC | AAGAGGCCTT | CCTCACTTTC | CTCTGTGTGA | TGTGTATCTG | CAGCCTGATC | 180 |
| 50 | GGTGCCATGG | CAAGACACCC | TCAGTCATCA | TCCTCATCAG | GACAGTCAGC | CCTGAACTCA | 240 |
| | AGTCTTACGC | TTTGGGAGTT | CTTTTTCTCC | TCCTTCGTTT | GTTGGGCTTC | ATCCCTCCAC | 300 |
| 35 | CCCTCATCTT | CGGGGCTGGC | ATCGACTCCA | CCTGCCTGTT | CTGGAGCACG | TTCTGTGGGG | 360 |
| | AGCAAGGCGC | CTGCGTCCTC | TACGACAATG | TGGTCTACCG | ATACCTGTAT | GTCAGCATCG | 420 |
| 40 | CCATCGCGCT | CAAATCCTTC | GCCTTCATCC | TGTACACCAC | CACGTGGCAG | TGCTGAGGAA | 480 |
| 10 | AAACTATAAA | CGCTACATCA | AAAACCACGA | GGCGGGCTG | AGCACCAGTG | AGTTCTTTGC | 540 |
| | CTCTACTCTG | ACCCTAGACA | ACCTGGGGAG | GGACCCTGTG | CCCGCAAACC | AGACACATAG | 600 |
| 45 | GACAAAGTTT | ATCTATAACC | TGGAAGACCA | TGAGTGGTGT | GAAAACATGG | AGTCCGTTTT | 660 |
| | ATAGTGACTA | AAGGAGGCT | GAACTCTGTA | TTAGTAATCC | AAGGGTCATT | TTTTTCTTAA | 720 |
| 50 | AAAAAGAAAA | AAAGGTTCCA | AAAAAAACCA | AAACTCAGTA | CACACACACA | GGCACAGATG | 780 |
| | CACACACACG | CAGACAGACA | CACCGACTTT | GTCCTTTTTC | TCAGCATCAG | AGCCAGACAG | 840 |
| | GATTCAGAAT | AAGGAGAGAA | TGACATCGTG | CGGCAGGGTC | CTGGAGGCCA | CTCGCGCGGC | 900 |
| 55 | TGGGCCACAG | AGTCTACTTT | GAAGGCACCT | CATGGTTTTC | AGGATGCTGA | CAGCTGCAAG | 960 |
| | CAACAGGCAC | TGCCAAATTC | AGGGAACAGT | GGTGGCCAGC | TTGGAGGATG | GACATTTCTG | 1020 |
| 60 | GATACACATA | CACATACAAA | ACAGAAAACA | AAAATTTTTTT. | . GAAGTTTCCT | AAAATAAAA | 1080 |

| | ААААААА | 1089 |
|----|--|-------------|
| 5 | (2) INFORMATION FOR SEQ ID NO: 39: | |
| 10 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 629 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39: | |
| 13 | AGCTCAGTTC CCTTAGAAAT GAAATTTTAA ATGACACTAC CAGGTAAGCC ACTGAGACCA | 60 |
| | GTGGAGGTGA TAGCTAAGAA CATAAGGAAT TAAGAATTTT TAATGGAGAA AGGAGGTAAT | 120 |
| 20 | GAATACCAGT TACATCCTAA GACTCACTGT AGTGGTGAGT GTTGTAATTT ATCTCGCTAT | 180 |
| | CCATCCTCTT TTAAGTTTTT CCTTAGAAAG TCCTCTATTG GTACCTTGGA GGGACTGCTG | 240 |
| 25 | TCAAAATATA TGGAAAAGTG GGTCTGTGTG GTACAAGAGG TGGACTTTGC CACACATGGA | 300 |
| | AGTTTGCTGC CAAGATCTTC ACTAATGAAA GAAATCACCA GTGAGCTGCA CAGATTAGCC | 360 |
| | AAATACTGAG CTCATTAGAA CTACTAAGGC CTGGACATTT CTGCCTAATC CAGGACTCCT | 4 20 |
| 30 | GTAATTATCA GTCTTTGCTT TGGAGCTTCC CATTGTGTAG CTGARAATTT GTCATATCTG | 4 80 |
| | CATTATAATC TAAGGCTCCA CATACTTAAT CCTGCTTCTC CCCCTTTTC TTTCCCTTTC | 540 |
| 35 | CCAGCGGTCA GCTCTGCTGC ATAGTCTGAA GACTTTCCCT GCCCAATCCT GATAAAATTC | 600 |
| 55 | TTGCACTCGT AACCCCATCT CAGTGTCTG | 629 |
| 40 | (2) INFORMATION FOR SEQ ID NO: 40: | |
| 45 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1964 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 50 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40: | |
| 50 | AAGAAGACAT GGAAATTGCT GAAGGATGTT TCAGGCATAT TAAGAAAATC TTTACGCAGC | 60 |
| | TTGAGGAATT CAGAGCCTCT GAATTGCTTC GAAGTGGACT GGACAGATCT AAATACCTTT | 120 |
| 55 | TAGTGAAAGA AGCCAAAATT ATTGCTATGA CCTGTACTCA TGCTGCCTTA AAACGACATG | 180 |
| | ACTTGGTCAA GCTAGGTTTC AAGTATGACA ACATTTTGAT GGAAGAGGCT GCTCAGATTC | 240 |
| 60 | TGGAGATAGA AACTTTTATC CCTCTTCTTC TACAGAATCC TCAGGATGGA TTTAGCCGAC | 300 |

| | TAAAACGATG | GATTATGATT | GGCGATCATC | ACCAGTTACC | TCCAGTTATT | AANGAACATG | 360 |
|----|------------|--------------|------------|------------|--------------|--------------|------|
| | GCCTTTCAAA | AGTACTCAAA | CATGGAGCAG | TCTCTCTTCA | CTCGCTTTGT | TCGCGTTGGA | 420 |
| 5 | GTTCCGACTG | TTGACCTTGA | TGCTCAAGGG | AGAGCCAGAG | CAAGCTTGTG | CAMCTNCTAC | 480 |
| | AACTGGCGAT | ACAAGAATCT | AGGAAACTTA | CCCCATGTGC | AGCTCTTGCC | AGAGTTTAGT | 540 |
| 10 | ACAGCAAATG | CTGGCTTACT | GTATGACTTC | CAGCTCATTA | ATGTTGAAGA | TTTTCAAGGA | 600 |
| ıu | GTGGGAGAAT | CTGAACCTAA | TCCTTACTTC | TATCAGAATC | TTGGAGAGGC | AGAATATGTA | 660 |
| | GTAGCACTTT | TTATGTACAT | GTGTTTACTT | GGTTACCCTG | CTGACAAAAT | CAGTATTCTA | 720 |
| 15 | ACAACATATA | ATGGCCAAAA | GCATCTTATT | CGCGACATCA | TCAATAGACG | ATGTGGAAAC | 780 |
| | AATCCATTGA | TTGGAAGACC | AAACAAGGTG | ACAACTGTTG | ATAGATTTCA | AGGTCAACAG | 840 |
| 20 | AATGACTATA | TTCTTCTTTC | TCTGGTACGA | ACCAGGGCAG | TGGGCCATCT | GAGGGATGTC | 900 |
| 20 | CGTCGCTTGG | TAGTGGCCAT | GTCTAGAGCC | AGACTTGGAC | TTTATATCTT | CGCCAGAGTA | 960 |
| | TCCCTCTTCC | AAAACTGTTT | TGAACTGACT | CCAGCTTTCA | GTCAGCTCAC | AGCTCGCCCC | 1020 |
| 25 | CTTCATTIGC | ATATAATTCC | AACAGAACCT | TTCCCAACTA | CTAGAAAGAA | TGGAGAGAGA | 1080 |
| | CCATCTCATG | AAGTACAAAT | ТАААААТАА | ATGCCCCAGA | TGGCAAACTT | TGTATACAAC | 1140 |
| 30 | ATGTACATGC | ATTTGATACA | GACTACACAT | CATTATCATC | AGACTTTATT | ACAACTACCA | 1200 |
| 30 | CCTGCTATGG | TAGAAGAGGG | TGAGGAAGTT | CAAAATCAAG | AAACAGAATT | GGAAACAGAA | 1260 |
| | GAAGAGGCCA | TGACTGTTCA | AGCTGACATC | ATACCCAGTC | CAACAGACAC | CAGCTGCCGT | 1320 |
| 35 | CAAGAAACTC | CAGCCTTTCA | AACTGACACC | ACCCCCAGTG | AGACAGGAGC | CACTTCCACT | 1380 |
| | CCAGAAGCCA | TCCCTGCTTT | ATCTGAGACC | ACCCCTACTG | TGGTAGGAGC | TGTATCTGCA | 1440 |
| 40 | CCGGCAGAAG | CTAACACACC | TCAGGATGCC | ACATCTGCCC | CAGAAGAGAC | CAAGTAGCCA | 1500 |
| 40 | AACTGTAGTC | : CTTCTAAAGG | AGGACATGGC | AGTCAAAAAG | TCTGAGTAAA | GCTGTTTTTT | 1560 |
| | GTATTTTATA | TTTGCTTCTG | CCATTTTACT | GTCACTÁATT | AATGTTTAGT | TCTTATATTT | 1620 |
| 45 | GTTAACTGAT | TTCGGTGTCT | TGAATATATT | TTTTTAAATT | ATGTGTATGA | ACAATTCTAG | 1680 |
| | TTTCATTTGT | TCAATCAGAA | GAGCAAATAA | CCATTCCTT | CATGTTTTGA | TCACTGAGTG | 1740 |
| 50 | TGTCTGTAAT | CATACCTAC | TTAAAATCAT | TTTCTATGA | TATATATAT A | ATACTTCACA | 1800 |
| 50 | TTTTTAGTG | A ACTTCTCTA | AGAAGAGGAC | AGAATATACI | r GGACTTAACO | ACGAATACCC | 1860 |
| | TTGAGTGTC | C AAATTGGGAA | GGAACTKGTI | TCTTCYGTT | A TACTAYCAA? | A TGCTTAAATT | 1920 |
| 55 | CKGTTTCCT | r TTTTCTTACO | TTTGTTTGCT | GTCTTTATG | r aaag | | 1964 |

^{60 (2)} INFORMATION FOR SEQ ID NO: 41:

196

(i) SEQUENCE CHARACTERISTICS:

5

(A) LENGTH: 1522 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

| | | _ | | _ | | | |
|----|------------|------------|------------|------------|------------|------------|------|
| 10 | CGTGTCCGCG | CGCCTGGGAG | ACGCTGCCTC | GGCCCGGACG | CGCCCGCGCC | CCCGCGGCTG | 60 |
| | GAGGGTGGTC | GCCACTGGGA | CACTGTGAAC | CAGGAGTRAG | TCGGAGCTGC | CGCGCTGCCC | 120 |
| 15 | AGGCCATGGA | CTGTGAGGTC | AACAACGGTT | CCAGCCTCAG | GGATGAGTGC | ATCACAAACC | 180 |
| 13 | TACTGGTGTT | TGGCTTCCTC | CAAAGCTGTT | CTGACAACAG | CTTCCGCAGA | GAGCTGGACG | 240 |
| | CACTGGGCCA | CGAGCTGCCA | GTGCTGGCTC | CCCAGTGGGA | GGGCTACGAT | GAGCTGCAGA | 300 |
| 20 | CTGATGGCAA | CCGCAGCAGC | CACTCCCGCT | TGGGAAGAAT | AGAGGCAGAT | TCTGAAAGTC | 360 |
| | AAGAAGACAT | CATCCGGAAT | ATTGCCAGGC | ACCTCGCCCA | GGTCGGGGAC | AGCATGGACC | 420 |
| 25 | GTAGCATCCC | TCCGGGCCTG | GTGAACGGCC | TGGCCCTGCA | GCTCAGGAAC | ACCAGCCGGT | 480 |
| 23 | CGGAGGAGGA | CCGGAACAGG | GACCTGGCCA | CTGCCCTGGA | GCAGCTGCTG | CAGGCCTACC | 540 |
| | CTAGAGACAT | GGAGAAGGAG | AAGACCATGC | TGGTGCTGGC | CCTGCTGCTG | GCCAAGAAGG | 600 |
| 30 | TGGCCAGTCA | CACGCCGTCC | TTGCTCCGTG | ATGTCTTTCA | CACAACAGTG | AATTTTATTA | 660 |
| | ACCAGAACCT | ACGCACCTAC | GTGAGGAGCT | TAGCCAGAAA | TGGGATGGAC | TGAACGGACA | 720 |
| 35 | GTTCCAGAAG | TGTGACTGGC | TAAAGCTCGA | TGTGGTCACA | GCTGTATAGC | TGCTTCCAGT | 780 |
| 33 | GTAGACGGAG | CCCTGGCATG | TCAACAGCGT | TCCTAGAGAA | GACAGGCTGG | AAGATAGCTG | 840 |
| | TGACTTCTAT | TTTAAAGACA | ATGTTAAACT | TATAACCCAC | TTTAAAATAT | CTACATTAAT | 900 |
| 40 | ATACTTGAAT | GAAAATGTCC | ATTTACACGT | ATTTGAATGG | CCTTCATATC | ATCCACACAT | 960 |
| | GAATCTGCAC | ATCTGTAAAT | CTACACACGG | TGCCTTTATT | TCCACTGTGC | AGGTTCCCAC | 1020 |
| 45 | TTAAAAATTA | AATTGGAAAG | CAGGTTTCAA | GGAAGTAGAA | ACAAAATACA | ATTTTTTGG | 1080 |
| 73 | TAAAAAAAA | TTACTGTTTA | TTAAAGTACA | ACCATAGAGG | ATGGTCTTAC | AGCAGGCAGT | 1140 |
| | ATCCTGTTTG | AGGAAAGCAA | GAATCAGAGA | AGGAACATAC | CCCTTACAAA | TGAAAAATTC | 1200 |
| 50 | CACTCAAAAT | AGGGACTATC | YATCTTAATA | CTAAGGAACC | AACAATCTTC | CTGTTTAAAA | 1260 |
| | AACCACATGG | CACAGAGATT | CNGAACTAAA | GTGCTGCACT | CAAATGATGG | GAAGTCCCGG | 1320 |
| 55 | CCCCAGTACA | CCAGGGGCTT | TGGACTTTTT | TCAACTTCGT | TTCCTTTTGT | TTGGANTCCA | 1380 |
| 55 | AAAGAACCAC | TTTGTGGTTC | TTAAAAGGGT | GTGAAGGTGA | TTTAAGGGGC | CCAGGTCAGC | 1440 |
| | CACTGGTTGG | TTTACAAAAT | CNGGGTAACT | AACTGCATAC | AACTTTTTCC | CNTTTCCATG | 1500 |
| 60 | NCATCAGGAC | TTTGCTAAAG | AC | | | | 1522 |

| 5 | (2) INFORMATION FOR SEQ ID NO: 42: | |
|----------|---|-----|
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 875 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42: | |
| 15 | TGGGATTTCC CTTTATCATG GAGGCCTTGT CCCACTTCCT CTATGTCCCT TTCCTTGGTG | 60 |
| | TCTGTGTCTG TGGGGCCATC TACACTGGCC TGTTCCTTCC TGAGACCAAA GGCAAGACCT | 120 |
| 20 | TCCAAGAGAT CTCCGAGGAA TTACACAGAC TCAACTTCCC CAGGCGGCC CAGGGCCCCA | 180 |
| 20 | CGTGGAGGAG CCTGGAGGTT ATCCAGTCAA CAGAACTCTA GTCCCAAAGG GGTGGCCGTA | 240 |
| | GCCAAAGCCA GCTACCGTCC TGTCCTCTGC TTCCTGCCAG GGCCCTGGTC CTCAMTYCCT | 300 |
| 25 | YCTGCATTCC TCATTTAAGG AGTGTTTATT GAGCACCCTT TGTGTGCAGA CATGGCTCCA | 360 |
| | GGTGCTTAGC AATCAWIGGT GAGCGTGGTA TCCAGGCTAA AGGTAATTAA CTGACAGRAA | 420 |
| 20 | ATCAGTAACA ACATAATTAC AGGYTGGTTG TGGCAGYTCA TGACTGTAAT CCCAGCACTT | 480 |
| 30 | TTGGGAGCCA AGGTGGGARG ATCAATTGAG GCCAGAGTTT GAAAMCAGCT AGGTAACATA | 540 |
| | GTGAGACCCC CTATCTCTAC AAAAAATTTT AAACATTAGC TGGGCATGGT GGTATGTGCT | 600 |
| 35 | AACAGCTCTA GCTACTCAGG AGGCTGAGGC AGCAGGATCA CTTGAGTCCA AGAGTTCAAG | 660 |
| | GTAGCAGTAA GCTACAATCA CACCACTGCA TGCCAGACTG GGTGACAGAG GGAGACTTCA | 720 |
| 40 | TCTCTTTAAA ACATAATAAT AATAATTACA GACTCAGGAA ATGCAGTGAA AGAAAAATAC | 780 |
| 40 | AGGTTGGCCA GGTGAGGTGG CTGATGCCTG TAATCCCAGC ACTTTGGGAG GCCAAGATGG | 840 |
| | GAAGATTGCT TTGAGACCAG AAGTTTGAGA CCAGC | 875 |
| 45 | | |
| | | |
| | (2) INFORMATION FOR SEQ ID NO: 43: | |
| 50 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 843 base pairs | |
| | (B) TYPE: nucleic acid(C) STRANDEDNESS: double | |
| 55 | (D) TOPOLOGY: linear | |
| <i>.</i> | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43: | |
| | CCCACGCGGT CCGNATCGTC CTTCCCTCAC TTCAGAGGGT GGCCAGAGCT GAATACCCAG | 60 |
| 60 | ACAGGARAN CONTROL ACOUNTED AND CONTROL OF AMERICANC CONCENTRATION | 120 |

420

480

| | CACCTGACAG | TTACAGAGGA | AACCCGCACC | CAGAATGCAC | GTGCTGTCTT | ATGGGAACAC | 180 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 5 | TCAGCGCAGA | GTGCTCAGGT | CCGGCCACAC | TCGGGCTGTG | CTTGGTCGTG | CCATGGAATT | 240 |
| 3 | CCTCAGGACT | TTCTCAGCCT | CCCTAATGGC | AGAAGCCCCT | TTACAGCAAG | ACATTTACCG | 300 |
| | TTTGTCTGAA | AATAGCCGAA | CTGAGCTTTT | CTTCAGGCTA | TATGAGAAGT | CTCTAGACAG | 360 |
| 10 | TGGGCACCGT | CAGAAAGCCC | AGAGCCTTGT | GATAGCTCCC | ACCCTGCCTG | GCTCAGATCT | 420 |
| | TCCCATTTT | TTTCCTCTGG | CACTAACCTC | ACCTTTTGTT | TTTTTGTGTT | TGTGTTTGTT | 480 |
| 15 | TTTGTTTTTG | CAGAGTTGGA | TTACAGAAAC | TCCTATGAAA | TTGAATATAT | GGAGAAAATT | 540 |
| 13 | GGCTCCTCCT | TACCTGTAAG | TTCGTCTGCC | TCGGGCCACT | TAGGGGACTC | GCTTTCCTGC | 600 |
| | CTTCAGGGGC | CTCCTCCCCT | GTGCAGAGTG | TCTCTGGGAG | CTCAGACCCC | AAATCGAGTG | 660 |
| 20 | TTTTCTGTGT | ACACAGCTTC | CCGGGTGCAC | AGCAATGATG | GACTGGGGCT | GGGGGTTGA | 720 |
| | GGTTTGTACT | CAATCCACTT | CGTTTGACAT | TTTCAGGGAG | AAAATGATAG | AATACAATTA | 780 |
| 25 | GACGTCCTGC | AGAATTACTT | TCCTAGACTG | AGAAAGAGCT | AGAGATTTCT | TTAAAAAAA | 840 |
| | AAA | | | | | | 843 |

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(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 489 base pairs (B) TYPE: nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

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CTCTTAGGCT TTGAAGCATT TTTGTCTGTG CTCCCTGATC TTCAGGTCAC CACCATGAAG 60 TTCTTAGCAG TCCTGGTACT CTTGGGAGTT TCCATCTTTC TGGTCTCTGC CCAGAATCCG 120

45 ACAACAGCTG CTCCAGCTGA CACGTATCCA GCTACTGGTC CTGCTGATGA TGAAGCCCCT 180

ACCGCTGCTT CTACCACTGC TCGTAAAGAC ATTCCAGTTT TACCCAAATG GGTTGGGGAT

ACAACTATTC ATGCTTCCTG TGATTTCATC CAACTACTTA CCTTGCCTAC GATATCCCCT

TTATCTCTAA TCAGTTTATT TTCTTTCAAA TAAAAAATAA CTATGAGCAA CAAAAAAAA

GATGCTGAAA CCACTGCTGC TGCAACCACT GCGACCACTG CTGCTCCTAC CACTGCAACC 240

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CTCCCGAATG GTAGAGTGTG TCCCTGAGAT GGAATCAGCT TGAGTCTTCT GCAATTGGTC 360

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PCT/US98/05311

199

| | (2) INFORMATION FOR SEQ ID NO: 45: | |
|----|---|-----|
| 5. | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 534 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 10 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45: | |
| | GAAGCAGTGT GTATCTATGA TTATATCTCT GTTCATCTAT ATATTTTTGA CATGTAGCAA | 60 |
| 15 | CACCTCTCCA TCTTATCAAG GAACTCAACT CGGTCTGGGT CTCCCCAGTG CCCAGTGGTG | 120 |
| 15 | GCCTTTGACA GGTAGGAGGA TGCAGTGCTG CAGGCTATTT TGTTTTTTGT TACAAAACTG | 180 |
| | TCTTTTCCCT TTTCCCCTCC ACCTGATTCA GCATGATCCC TGTGAGCTGG TTCTCACAAT | 240 |
| 20 | CTCCTGGGAC TGGGCTGAGG CAGGGGCTTC GCTCTATTCT CCCTAACCAT ACTGTCTTCC | 300 |
| | TTTCCCCTTG CCACTTAGCA GTTATCCCCC CAGCTATGCC TTCTCCCTCC CTCCCTTGCC | 360 |
| 25 | CTGGCATATA TTGTGCCTTA TTTATGCTGC AAATATAACA TTAAACTATC AAGTGAAAAA | 420 |
| 23 | AAAAAAAAA AAAACTCCAA GGGGGGCCG GTACCCAATT CCCCCTATAN TGAGTCNTAT | 480 |
| | TACAATTCAC TGGGCCGTCG TTTTACAACG TCGTGAATGG GAAAACCTGG GCGT | 534 |
| 30 | | |
| | (2) INFORMATION FOR SEQ ID NO: 46: | |
| 35 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1374 base pairs (B) TYPE: nucleic acid | |
| 40 | (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46: | |
| | GGCACGAGTC CGGGATGAGC TCAGCCGCGG CCGACCACTG GGCGTGGTTG CTGGTGCTCA | 60 |
| 45 | GCTTCGTGTT TGGATGCAAT GTTCTTAGGA TCCTCCTCCC GTCCTTCTCA TCCTTCATGT | 120 |
| | CCAGGGTGCT GCAGAAGGAC GCGGAGCAGG AGTCACAGAT GAGAGCGGAG ATCCAGGACA | 180 |
| 50 | TGAAGCAGGA GCTCTCCACA GTCAACATGA TGGACGAGTT TGCCAGATAT GCCAGGCTGG | 240 |
| 50 | AAAGAAAGAT CAACAAGATG ACGGATAAGC TCAAAACCCA TGTGAAAGCT CGGACAGCTC | 300 |
| | AATTAGCCAA GATAAAATGG GTGATAAGTG TCGCTTTCTA CGTATTGCAG GCTGCCCTGA | 360 |
| 55 | TGATCTCACT CATTTGGAAG TATTATTCTG TCCCTGTGGC TGTCGTGCCG AGTAAATGGA | 420 |
| | TAACCCCTCT AGACCGCCTG GTAGCCTTTC CTACTAGAGT AGCAGGTGGT GTTGGAATTA | 480 |
| | CCTGTTGGAT TTTAGTCTGT AACAAAGTTG TCGCTATTGT GCTTCATCCG TTCAGCTGAA | 540 |

200

| | CAGGAGGATG | GATACAGCCG | CGAGGCTAAA | AAACGGATTT | CCTCTTCCTA | GCTTAAAATC | 600 |
|----|------------|--------------|--|------------------|------------|------------|------|
| | TGATTTACAC | TGTTTTGTTT | TTTAAGAAAC | AAAAGTGCAT | AGTTTAGATT | TTTTTTTTG | 660 |
| 5 | TTGAATATGT | TIGTTCTTGG | ACTTTATGAG | AGAGTCTTAT | AAGAATCACG | ATTTTCTACA | 720 |
| | CCTGTCATTG | AGCCAAGAAA | GTCCAGTTTA | TGACACGTAT | GTACTAGTGA | ACACCGTCCT | 780 |
| 10 | CGATCTGTAC | GAAATGTGAA | ATGTTTAGGG | ACATCTCCAT | GCTGTCACTT | GTGATTTGCC | 840 |
| 10 | CTCTTATGTA | TTTTGGTCAT | ATTGCCAACT | GGAAAGTCAA | AATTTTCTAA | CAACTTTAAG | 900 |
| | TAAGTTCTTT | GAAGACTTAG | TGCTGTTTTT | AATCCAGTTT | AGAAAGTAAC | TTAATTTTAA | 960 |
| 15 | TACCACTACT | AAAAATTCGA | AAATTTCTTC | TTTAATCACA | TTCAATATGG | TTAAAAGAAC | 1020 |
| | AACACTAATT | GACATTGCGT | GGGCTTTTTC | TCCCTTTGTT | TAAAATGTCA | TTTGTTGAGC | 1080 |
| 20 | AAGAGTTGTA | TAGTATTATC | TACTTACTTG | AGGCTGTTAA | TTTTTCATTA | CAGTGTTTTG | 1140 |
| 20 | TAAATGTATC | CACGAGACCA | TGATGCATTG | TTTTGTGCTC | AACTTGTGTT | TTGTATTTAA | 1200 |
| | AGCATTTTGA | ATGAAGTGTA | TTTTATAAGC | ATTTAATATT | TATGCTCTTT | AGAATGGAAC | 1260 |
| 25 | ACAGAAAACA | AACCTTATAA | GTCCTGATTA | ATCTGAACCA | ATAACCTGTG | TGGCCTACAA | 1320 |
| | AGTATAATTC | TATTAAATGT | TCCTTAAAAC | ааааааааа | АААААААА | AAAA | 1374 |
| 30 | | | | | | | |
| | (2) INFORM | ATION FOR SI | EQ ID NO: 4 | 7: | | | |
| 35 | (i) | (B) TYP | HARACTERIST GTH: 596 ba E: nucleic | se pairs acid | | | |

(D) TOPOLOGY: linear

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

| GAATTCGNCA | CGAGATTACT | TGGACATGAA | AGAACTCAGG | TTCAAGTTTA | TTCATTTACT | 60 |
|------------|------------|------------|------------|------------|------------|-----|
| AAGTTAGTTA | AATCATGTGC | CTTCCATGAG | CCTTCATTTG | GTAACTTGGA | AAATGGAAAT | 120 |
| AATAACACTA | GTCATATATA | TTCTACACTG | CTACCATATG | GACCAAAGGG | ATTATAGATT | 180 |
| ACAATCACCA | TCATTCCTGC | TGACAGGTAT | ATAGAAAACA | ATTTCATTGA | AGAAAAGTCC | 240 |
| TTACATTTAT | CCTTTTCCTA | ATATCTGCAT | GGGTAAACTA | ATAAATATAG | TCATTAGAAA | 300 |
| ACCCTTATTA | TTATTATTAG | TTCAATGTGA | GAACTGCTGC | AGAAAAAATA | TGCTTTATAA | 360 |
| TATTITCTTG | AATATACATA | ATATTCATAA | ATTTCAAAT | CATTGAAAAT | TACCTTAAAA | 420 |
| TTGGAAAAAA | TGTGCATTTC | TACTCATATA | ACAGTATAAA | ATTCCTATGT | CAATCTCTTT | 480 |
| TTTTTTTT | TGTTTTGAGT | TGGAGTCTCG | CTCTGTCGCC | CAGGCTGGGC | AACAGAGCAG | 540 |
| GACCCTGTCT | ТААТТАААА | АААААААА | AAACTCGAGG | GGGCCCGGT | ACCCTA | 596 |

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| 5 | (2) INFORMATION FOR SEQ ID NO: 48: | |
|----------|---|-----|
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 851 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48: | |
| 15 | CACATGAAGA CACACAGTGG TGAGAAGCCC TTCCGCTGCG CCCGCTGTCC TTATGCCTCT | 60 |
| | CCTCATCTGG ATAACCTGAA ACGGCACCAG CGCGTCCATA CAGGAGAGAA GCCCTACAAG | 120 |
| 20 | TGCCCCCTCT GCCCTTATGC CTGTGGCAAT CTGGCCAACC TCAAGCGTCA TGGTCGCATC | 180 |
| 20 | CACTCTGGTG ACAAACCTTT TCGGTGTAGC CTTTGCAACT ACAGCTGCAA CCAGAGCATG | 240 |
| | AACCTCAAAC GTCACATGCT GCGGCACACA GGCGAGAAGC CTTCCGCTGT GCCACCTGCG | 300 |
| 25 | CCTATACCAC GGGCCACTGG GACAACTACA AGCGCCACCA GAAGGTGCAT GGCCACGGTG | 360 |
| | GGGCAGGAGG GCCTGGTCTC TCTGCCTCTG AGGGCTGGGC CCCACCTCAT AGCCCACCCT | 420 |
| 30 | CTGTTTTGAG CTCTCGGGGC CCACCAGCCC TGGGGACTGC TGGCAGCCGG GCTGTCCACA | 480 |
| 30 | CAGACTCATC CTGAACTAGG TCCTTCTTCC CCATGTTTTA TACAGACGGA CCAGAAGCCA | 540 |
| | CCTTTTTCTC CCCCGCTGGC CAGGGGCTCC ACACAGACTA ACGTAGGCAC TATAAGGACC | 600 |
| 35 | AGCCCAACCC CATGGGCGGG GGGCCCCATA TGGACCAGGG GACCTTGCCT TGACTGAGGC | 660 |
| | ACTTCACGAG CTCAGTGAGA AGGGCCCTGT ATTCACCTCC ACTGCCCCCA GGGGCTGTGG | 720 |
| 40 | ACAAACCGGC TGGGGGACTG CCCAGCCTCC CACCTGTTTA TTTAACTTAT TTCAGTGCTT | 780 |
| 70 | TATAATAAAG GAAACACTAA CAAAGCCATG TCTATGCTGA ATTGGCAATG GCAGGCAATT | 840 |
| | TGGCCTTACC C | 851 |
| 45 | | |
| | (2) INFORMATION FOR SEQ ID NO: 49: | |
| 50 55 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 2020 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49: | |
| | GTGAAATGAA AACAGTCTTT TTATAGCCTT TAGCTTGTGA GTTTGGAAGT TTGGGGGGTC | 60 |
| 60 | TTATGTTTGT TTTGCCTCTT CTGTTTCTTG GAGGAGAGTT GAGGCTTTTC TTAGGTGCAT | 120 |

| | ACACAGACCC | AGGTGAACAC | GCTGACTGTG | AACCTGCCCT | GTATCCGGAG | CTGTGCTGGG | 180 |
|------------|------------|------------|------------|---------------------|------------|------------|------|
| 5 | CACTGAGGGG | ATGCAACAAA | ATTAGGAGAG | GWTCCTTGCT | CCCAACGTCT | ACTTCTCCTA | 240 |
| <i>J</i> . | CCTCAACAGG | GGTCCAGGGT | GCAGTGAACT | CAGTTCTTGG | CCCTTGGGTG | AGGATTCATG | 300 |
| | GATGAATGAA | AGCTAGACCT | GATGGGGAGG | CATTATGACT | AAATAGGCCC | AGCCTCCTTC | 360 |
| 10 | CCTTCCAGCT | CTGTCCTAGG | AGCATAGGCG | GGAAATCTGA | GTAGAGTCTG | ACTGCAGTTT | 420 |
| | TTGCTTATGA | TTTGTAAAAG | CCGTCATGGG | GTCAA T AAGA | AAATAGGGGT | GATGGAGGG | 480 |
| 15 | GAGAAGCCCA | GGACTGGGAG | AATCGCACGT | GCCCCAGGGG | TTTTCACCAA | GGATTTTCAA | 540 |
| 13 | GACAAACTGG | AGTAAGAATT | AAAGCCCCAG | AGGATTTAAT | TATCCTGGTT | TGCAAAAGAG | 600 |
| | CCTCCCATGC | CAGTACCGCC | CAGCCTTGGA | GGCCGGAATG | CTCATGGCCC | CTGTGGTCTG | 660 |
| 20 | CTTGTCCTTC | AGCCCATGCC | CAGCAGATAC | CTCTCTGACT | GGAGACGGGC | TCAAAGCTGG | 720 |
| | ATTAGAAAGG | GGAGMGGCAC | TTGTGACTTT | GTTTGACTCT | GTGACTCACT | TCCTCGCTCA | 780 |
| 25 | CACCTTGTTT | GAACTACTGG | ACTTTCAACT | GGCTTTCCTT | AGGTCAGGCA | AGCAGACAGC | 840 |
| | TCCCCACTGA | AGAGGTCTGT | ACAGTGACAA | ccceeeccee | CAGCAAGGAC | ACAGATGCAG | 900 |
| | CCACAGTAAG | GCTCCATCAG | GACTGGGTCA | GTGATGGCAA | CAGGATGGCC | AAGGATGGCT | 960 |
| 30 | CTAGAACAYT | CTGTCCATGC | GTCACTCCCC | CCAGTTTTRT | TTTTAGCTTT | GGCTTCAGGG | 1020 |
| | AGTGACAGCC | ATCACAAATA | GCCACATTCT | GCTCTACTCT | CCAACATACC | AGATTSTACA | 1080 |
| 35 | CTGTTGTTAT | TTCATGAGAC | GTGAATGTTG | CAGAGAGTGG | GGGGATTCTG | GTTGTTAAGG | 1140 |
| | AACTTACACT | GGGGAGCTTT | ACTCTTCCGT | GTCAACAATG | TGACTACATG | TTCTCCAGAT | 1200 |
| | TAGCCACACA | TGCAAACATC | AGTGTCCTTC | TAGCTTTANC | CGAGAAAGAA | ACCAGTCCCA | 1260 |
| 40 | GGGAATGAAT | GGTGGTCTCC | CCACTCCCGG | CAGCACTTTA | GGCAGCCCAT | AAGCTATGCG | 1320 |
| | AGAATGTGAA | CGCTCACCTT | GCTCCGTCAC | GGTTCTGACC | TACCACATAA | ACAGGAAGAA | 1380 |
| 45 | GCCAGTGACC | GGAACAGCTC | TAGGAATAAC | AAGTCAGAAT | AGAAGTGTCC | TTTATATTAC | 1440 |
| 15 | CAGAAAATAT | GGGCTTGGCC | TAAGTCGCTG | TCTCCTAACC | TGCCGGGGTC | ATTCCCCACC | 1500 |
| | AAACACCCCA | TACTAAGGAG | CCATGAGCCA | CCTGGACATT | CACCTTTTCT | TTGACCATCT | 1560 |
| 50 | GGAGTCTGGG | GCAACTTAAG | GAAGGCNCCA | CACAGTGGTG | CAGGCACATT | TCCAAGCGTA | 1620 |
| | GGTGTCCCTG | GCTTTTGTGG | CCAAAGCTAG | TGTTATGGTC | AACAACAGGC | CAGGGTCTGT | 1680 |
| 55 | GGGGCACTGA | CCTTGAAAGT | GGCAAAATGG | AGGTTTCACA | GGCTGTGCGG | GAGCAGGACG | 1740 |
| 55 | GCTTGCTTCA | TCTAACAATC | TCAGTTTCCT | TTAAAAAAAG | AAAGAAAGGA | AAAGATTTCA | 1800 |
| | TAAGCAGGTG | TCAGTGGACA | GTTTAAGYAC | TTAACCATTT | CTCTTTCTTC | TTATGGATGT | 1860 |
| 60 | GAACTGTGCT | GTGGATAAAT | CATTIGTATT | TCTTGAATGT | TCTCTATGAC | TAACAGTTAT | 1920 |

| | TAAGTCGGTT GTGTATATGT GTAACTAATG TAACTGCCTT TTAAAATTTC ATTACAATAA | 1980 |
|----|--|------|
| 5 | AAATGACTTT GCTCTGAAMA AAAAAAAAA AAAAACTCGA | 2020 |
| 10 | (2) INFORMATION FOR SEQ ID NO: 50: | |
| 15 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 2432 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50: | |
| 20 | ATGAAGGTC GTTGGTGGGA AAGATGGCGG CGACTCTGGG ACCCCTTGGG TCGTGGCAGC | 60 |
| 20 | AGTGGCGGCG ATGTTTGTCG GCTCGGGATG GGTCCAGGAT GTTACTCCTT CTTCTTTTGT | 120 |
| | TGGGGTCTGG GCAGGGGCCA CAGCAAGTCG GGGCGGGTCA AACGTTCGAG TACTTGAAAC | 180 |
| 25 | GGGAGCACTC GCTGTCGAAG CCCTACCAGG GTGTGGGCAC AGGCAGTTCC TCACTGTGGA | 240 |
| | ATCTGATGGG CAATGCCATG GTGATGACCC AGTATATCCG CCTTACCCCA GATATGCAAA | 300 |
| 30 | GTAAACAGGG TGCCTTGTGG AACCGGGTGC CATGTTTCCT GAGAGACTGG GAGTTGCAGG | 360 |
| 50 | TGCACTTCAA AATCCATGGA CAAGGAAAGA AGAATCTGCA TGGGGATGGC TTGGCAATCT | 420 |
| | GGTACACAAG GAATCGGATG CAGCCAGGGC CTGTGTTTGG AAACATGGAC AAATTTGTGG | 480 |
| 35 | GGCTGGGAGT ATTTGTAGAC ACCTACCCCA ATGAGGAGAA GCAGCAAGAG CGGGTATTCC | 540 |
| | CCTACATCTC AGCCATGGTG AACAACGGCT CCCTCAGCTA TGATCATGAG CGGGATGGGC | 600 |
| 40 | GGCCTACAGA GCTGGGAGGC TGCACAGCCA TTGTCCGCAA TCTTCATTAC GACACCTTCC | 660 |
| 70 | TGGTGATTCG CTACGTCAAG AGGCATTTGA CGATAATGAT GGATATTGAT GGCAAGCATG | 720 |
| | AGTGGAGGGA CTGCATTGAA GTGCCCGGAG TCCGCCTGCC CCGCGGCTAC TACTTCGGCA | 780 |
| 45 | CCTCCTCCAT CACTGGGGAT CTCTCAGATA ATCATGATGT CATTTCCTTG AAGTTGTTTG | 840 |
| | AACTGACAGT GGAGAGACC CCAGAAGAGG AAAAGCTCCA TCGAGATGTG TTCTTGCCCT | 900 |
| 50 | CAGTGGACAA TATGAAGCTG CCTGAGATGA CAGCTCCACT GCCGCCCCTG AGTGGCCTGG | 960 |
| 50 | CCCTCTTCCT CATCGTCTTT TTCTCCCTGG TGTTTTCTGT ATTTGCCATA GTCATTGGTA | 1020 |
| | TCATACTCTA CAACAAATGG CAGGAACAGA GCCGAAAGCG CTTCTACTGA GCCCTCCTGC | 1080 |
| 55 | TGCCACCACT TTTGTGACTG TCACCCATGA GGTATGGAAG GAGCAGGCAC TGGCCTGAGC | 1140 |
| | ATGCAGCCTG GAGAGTGTTC TTGTCTCTAG CAGCTGGTTG GGGACTATAT TCTGTCACTG | 1200 |
| 60 | GAGTTTGAA TGCAGGGACC CCGCATTCCC ATGGTTGTGC ATGGGGACAT CTAACTCTGG | 1260 |

| | TCTGGGAAGC | CACCCACCCC | AGGCAATGC | TGCTGTGATG | TGCCTTTCCC | TGCAGTCCTT | 1320 |
|----|------------|--------------|----------------------------|-------------|------------|------------|------|
| | CCATGTGGGA | GCAGAGGTGT | GAAGAGAATT | TACGTGGTTG | TGATGCCAAA | ATCACAGAAC | 1380 |
| 5 | AGAATTTCAT | AGCCCAGGCT | GCCGTGTTGT | TTGACTCAGA | AGGCCCTTCT | ACTTCAGTTT | 1440 |
| | TGAATCCACA | AAGAATTAAA | AACTGGTAAC | ACCACAGGCT | TTCTGACCAT | CCATTCGTTG | 1500 |
| 10 | GGTTTTGCAT | TTGACCCAAC | CCTCTGCCTA | CCTGAGGAGC | TTTCTTTGGA | AACCAGGATG | 1560 |
| 10 | GAAACTTCTT | CCCTGCCTTA | CCTTCCTTTC | ACTCCATTCA | TTGTCCTCTC | TGTGTGCAAC | 1620 |
| | CTGAGCTGGG | AAAGGCATTT | GGATGCCTCT | CTGTTGGGGC | CTGGGGCTGC | AGAACACACC | 1680 |
| 15 | TGCGTTTCAC | TGGCCTTCAT | TAGGTGGCCC | TAGGGAGATG | GCTTTCTGCT | TTGGATCACT | 1740 |
| | GTTCCCTAGC | ATGGGTCTTG | GGTCTATTGG | CATGTCCATG | GCCTTCCCAA | TCAAGTCTCT | 1800 |
| 20 | TCAGGCCCTC | AGTGAAGTTT | GGCTAAAGGT | TGGTGTAAAA | ATCAAGAGAA | GCCTGGAAGA | 1860 |
| 20 | CATCATGGAT | GCCATGGATT | AGCTGTGCAA | CTGACCAGCT | CCAGGTTTGA | TCAAACCAAA | 1920 |
| | AGCAACATTT | GTCATGTGGT | CTGACCATGT | GGAGATGTTT | CTGGACTTGC | TAGAGCCTGC | 1980 |
| 25 | TTAGCTGCAT | GTTTTGTAGT | TACGATTTTT | GGAATCCCAC | TTTGAGTGCT | GAAAGTGTAA | 2040 |
| | GGAAGCTTTC | TTCTTACACC | TTGGGCTTGG | ATATTGCCCA | GAGAAGAAAT | TTGGCTTTTT | 2100 |
| 30 | TTTTCTTAAT | GGACAAGAGA | CAGTTGCTGT | TCTCATGTTC | CAAGTCTGAG | AGCAACAGAC | 2160 |
| 50 | CCTCATCATC | TGTGCCTGGA | AGAGTTCACT | GTCATTGAGC | AGCACAGCCT | GAGTGCTGGC | 2220 |
| | CTCTGTCAAC | CCTTATTCCA | CTGCCTTATT | TGACAAGGGG | TTACATGCTG | CTCACCTTAC | 2280 |
| 35 | TGCCCTGGGA | TTAAATCAGT | TACAGGCCAG | AGTCTCCTTG | GAGGGCCTGG | AACTCTGAGT | 2340 |
| | CCTCCTATGA | ACCTCTGTAG | CCTAAATGAA | ATTCTTAAAA | TCACCGATGG | AACCAAAAAA | 2400 |
| 40 | ААААААААА | АААААААА | АААААААА | AA | | | 2432 |
| 45 | (2) INFORM | ATION FOR SI | EQ ID NO: 5 | l: | | | |
| | (i) | SEQUENCE CI | HARACTERIST GTH: 2340 b | | | | |
| | | | E: nucleic ANDEDNESS: | | | | |
| 50 | | (D) TOP | OLOGY: line | ar | | | |
| | (xi |) SEQUENCE | DESCRIPTION | : SEQ ID NO | : 51: | | |
| 55 | GACGCTGGGG | GCGGGTGGGG | GCGCGGGGTA | CCGGGCTGGA | ceecceecce | GCGCCCCCTC | 60 |
| 55 | ATTAGTATGC | GGACGAAGCG | GCGGGCTGCG | CGGAGNGACG | TCCCCTGCAG | CCGCGGACCG | 120 |
| | AGGCAGCGGC | GGCACCTGCC | GGCCGAGCAA | TGCCAAGTGA | GTACACCTAT | GTRAAACTGA | 180 |

GAAGTGATTG CTCGAGGCCT TCCCTGCAAT GGTACACCCG AGCTCAAAGC AAGATGAGAA 240

| | GGCCCAGCTT | GITATTAAAA | GACATCCTCA | AATGTACATT | GCTTGTGTTT | GGAGTGTGGA | 300 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | TCCTTTATAT | CCTCAAGTTA | AATTATACTA | CTGAAGAATG | TGACATGAAA | AAAATGCATT | 360 |
| 5 | ATGTGGACCC | TGACCATGTA | AAGAGAGCTC | AGAAATATGC | TCAGCAAGTC | TTGCAGAAGG | 420 |
| | AATGTCGTCC | CAAGTTTGCC | AAGACATCAA | TGGCGCTGTT | ATTTGAGCAC | AGGTATAGCG | 480 |
| 10 | TGGACTTACT | CCCTTTTGTG | CAGAAGGSCC | CCAAAGACAG | TGAAGCTGAG | TCCAAGTACG | 540 |
| | ATCCTCCTTT | TGGGTTCCGG | AAGTTCTCCA | GTAAAGTCCA | GACCCTCTTG | GAACTCTTGC | 600 |
| 15 | CAGAGCACGA | CCTCCCTGAA | CACTTGAAAG | CCAAGACCTG | TCGGCGCTGT | GTGGTTATTG | 660 |
| 13 | GAAGCGGAGG | AATACTGCAC | GGATTAGAAC | TGGGCCACAC | CCTGAACCAG | TTCGATGTTG | 720 |
| | TGATAAGGTT | AAACAGTGCA | CCAGTTGAGG | GATATTCAGA | ACATGTTGGA | ААТААААСТА | 780 |
| 20 | CTATAAGGAT | GACTTATCCA | GAGGGCGCAC | CACTGTCTGA | CCTTGAATAT | TATTCCAATG | 840 |
| | ACTTATTTGT | TGCTGTTTTA | TTTAAGAGTG | TTGATTTCAA | CTGGCTTCAA | GCAATGGTAA | 900 |
| 25 | AAAAGGAAAC | CCTGCCATTC | TGGGTACGAC | TCTTCTTTTG | GAAGCAGGTG | GCAGAAAAA | 960 |
| 23 | TCCCACTGCA | GCCAAAACAT | TTCAGGATTT | TGAATCCAGT | TATCATCAAA | GAGACTGCCT | 1020 |
| | TTGRACATCC | TTCAGTACTC | AGAGCCTCAG | TCAAGGTTCT | GGGGCCGAG | ATAAGAACGT | 1080 |
| 30 | CCCCACAATC | GGTGTCATTG | CCGTTGTCTT | AGCCACACAT | CTGTGCGATG | AAGTCAGTTT | 1140 |
| | GGCGGGTTTT | GGATATGACC | TCAATCAACC | CAGAACACCT | TTGCACTACT | TCGACAGTCA | 1200 |
| 35 | ATGCATGGCT | GCTATGAACT | TTCAGACCAT | GCATAATGTG | ACAACGGAAA | CCAAGTTCCT | 1260 |
| 55 | CTTAAAGCTG | GTCAAAGAGG | GAGTGGTGAA | AGATCTCAGT | GGAGGCATTG | ATCGTGAATT | 1320 |
| | TTGAACACAG | AAAACCTCAG | TTGAAAATGC | AACTCTAACT | CTGAGAGCTG | TTTTTGACAG | 1380 |
| 40 | CCTTCTTGAT | GTATTTCTCC | ATCCTGCAGA | TACTTTGAAG | TGCAGCTCAT | GTTTTTAACT | 1440 |
| | TTTAATTTAA | AAACACAAAA | AAAATTTTAG | CTCTTCCCAC | TTTTTTTTC | CTATTTATTT | 1500 |
| 45 | GAGGTCAGTG | TTTGTTTTTG | CACACCATTT | TGTAAATGAA | ACTTAAGAAT | TGAATTGGAA | 1560 |
| 75 | AGACTTCTCA | AAGAGAATTG | TATGTAACGA | TGTTGTWTTG | ATTTTTAAGA | AAGTAATTTA | 1620 |
| | ATTTGTAAAA | CTTCTGCTCG | TTTACACTGC | ACATTGAATA | CAGGTAACTA | ATTGGAAGGA | 1680 |
| 50 | GAGGGGAGGT | CACTCTTTTG | ATGGTGGCCC | TGAACCTCAT | TCTGGTTCCC | TGCTGCGCTG | 1740 |
| | CTTGGTGTGA | CCCACGGAGG | ATCCACTCCC | AGGATGACGT | GCTCCGTAGC | TCTGCTGCTG | 1800 |
| 55 | ATACTGGGTC | TGCGATGCAG | CGGCGTGAGG | CCTGGGCTGG | TTGGAGAAGG | TCACAACCCT | 1860 |
| 55 | TCTCTGTTGG | TCTGCCTTCT | GCTGAAAGAC | TCGAGAACCA | ACCAGGGAAG | CTGTCCTGGA | 1920 |
| | GGTCCCTGGT | CGGAGAGGGA | CATAGAATCT | GTGACCTCTG | ACAACTGTGA | AGCCACCCTG | 1980 |
| 60 | GGCTACAGAA | ACCACAGTCT | TCCCAGCAAT | TATTACAATI | CTTGAATTCC | TTGGGGATTT | 2040 |

| | TTTACTGCCC TTTCAAAGCA CTTAAGTGTT AGATCTAACG TGTTCCAGTG TCTGTCTGAG | 2100 |
|----|---|------|
| 5 | GTGACTTAAA AAATCAGAAC AAAACTTCTA TTATCCAGAG TCATGGGAGA GTACACCCTT | 2160 |
| 5 | TCCAGGAATA ATGTTTTGGG AAACACTGAA ATGAAATCTT CCCAGTATTA TAAATTGTGT | 2220 |
| | ATTTAAAAAA AAGAAACTTT TCTGAATGCC TACTGGCGGT GTATACCAGG CAGTGTGCCA | 2280 |
| 10 | GTTTAAAAAG ATGAAAAAGA ATAAAAACTT TTGAGGAAMA AAAAAAAAAA AAAAACTCGA | 2340 |
| | | |
| 15 | (2) INFORMATION FOR SEQ ID NO: 52: | |
| 20 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 601 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52: | |
| 25 | AGTAGGGGAG ACTGAGACTG ACCGGTAGCC AGGCAGGCGG ACGACGCACG CCCGGACAGA | 60 |
| | CTGAGCAGGC GCCGGAGAAC CACTCACAGG TTCCCCCCGC CTTTCCCTTT GAAANCTAGG | 120 |
| 30 | CTTTTGCCTT TCCCGTGGCG CCCGAGAGAG AATGCTGGAC TCTGCCGACT TCAGCGCAAC | 180 |
| 50 | TAANGATTTC TCAAGCTAGG GGACAAACGA TCAGCCCAAT CCTGAGAAGG GGGGAACCAA | 240 |
| | GCACCCCGTC CCCATCCCCC TCCCCTCCCC CGACTAAACT CGGGCGCCAA ACCCAGCCCT | 300 |
| 35 | TCTCTAACCA CCCTACTTCC TCCTCTCCTT TCTAGCATGG TGGCTGTATG GACAGTCTGA | 360 |
| | CAGAACAGAG ACTGACATCT CCCAATCTGC CGGCCCCCCA CCTGGAACAC TACAGTGTTC | 420 |
| 40 | TGCATTGCAC CATGACCCTG GATGTGCAAA CTGTAGTCGT TTTTGCCGTG ATTGTAGTCC | 480 |
| | TCCTGCTTGT CAATGTCATA CTCATGTTTT TCCTGGGAAC GCGCTGAATG GAGTCCAGNC | 540 |
| | ACCTGAGCTG TCGCGAACTC TCGCTTTGAT TTCATCCCGA GAGCCACCGA GAAGAAAAA | 600 |
| 45 | A | 601 |
| | | |
| 50 | (2) INFORMATION FOR SEQ ID NO: 53: | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 359 base pairs | |
| 55 | (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53: | |
| 60 | CTCGTGCCGA ATTCGGCACG AGAGATGGTA CTTTTAAGAG GTAATTAGGT TGCTAAGATG | 60 |

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| | GATTAACATC | TTTCTCTTGA | CACTGAGACT | GGGTTCTCCT | GGGAATGGTT | AGTTCCCAAG | 120 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 5 | AGAGTGAGTT | GTTATAAAAC | AATGCTGCCT | CTTCTATTTT | GCGCTTTTTG | TTTGCACAAA | 180 |
| 3 | CTCGGTCCCC | TTCTGTTTCT | CTACGATGTT | TTGATGCRGC | ATGAGGCAGT | CATGAGAACC | 240 |
| | CACCAGATAC | AGCTGCCTGA | TCCTGAATTT | CCCAGCCAAC | AGAACCAAGT | GCTAAATAAA | 300 |
| 10 | ACTCTTTTTA | ATAAGTTAAA | АААААААА | АААААААА | AANAAANANA | АААААААА | 359 |

15 (2) INFORMATION FOR SEQ ID NO: 54:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1141 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

| 25 | GGCACGAGCT | GCTGAGGCGT | GAGAATGGCG | TCCCGCGGCC | GGCGTCCGGA | GCATGGCGGA | 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| | CCCCAGAGC | TGTTTTATGA | CGAGACAGAA | GCCCGGAAAT | ACGTTCGCAA | CTCACGGATG | 120 |
| 30 | ATTGATATCC | AGACCAGGAT | GGCTGGGCGA | GCATTGGAGC | TTCTTTATCT | GCCAGAGAAT | 180 |
| 50 | AAGCCCTGTT | ACCTGCTGGA | TATTGGCTGT | GGCACTGGGC | TGAGTGGAAG | TTATCTGTCA | 240 |
| | GATGAAGGGC | ACTATTGGGT | GGGCCTGGAT | ATCAGCCCTG | CCATGCTGGA | TGAGGCTGTG | 300 |
| 35 | GACCGAGAGA | TAGAGGGAGA | CCTGCTGCTG | GGGGATATGG | GCCAGGGCAT | CCCATTCAAG | 360 |
| | CCAGGCACAT | TTGATGGTTG | CATCAGCATT | TCTGCTGTGC | AGTGGCTCTG | TAATGCTAAC | 420 |
| 40 | AAGAAGTCTG | AAAACCCTGC | CAAGCGCCTG | TACTGCTTTT | TTGCTTCTCT | TTTTTCTGTT | 480 |
| 40 | CTCGTCCGGG | GATCCCGAGC | TGTCCTGCAG | CTGTACCCTG | AGAACTCAGA | GCAGTTGGAG | 540 |
| | CTGATCACAA | CCCAGGCCAC | AAAGGCAGGC | TTCTCCGGTG | GCATGGTGGT | AGACTACCCT | 600 |
| 45 | AACAGTGCCA | AAGCAAAGAA | ATTCTACCTC | TGCTTGTTTT | CTGGGCCTTC | GACCTTTATA | 660 |
| | CCAGAGGGGC | TGAGTGAAAA | TCAGGATGAA | GTTGAACCCA | GGGAGTCTGT | GTTCACCAAT | 720 |
| 50 | GAGAGGTTCC | CATTAAGGAT | GTCGAGGCGG | GGAATGGTGA | GGAAGAGTCG | GGCATGGGTG | 780 |
| 30 | CTGGAGAAGA | AGGAGCGGCA | CAGGCGCCAG | GGCAGGGAAG | TCAGACCTGA | CACCCAGTAC | 840 |
| | ACCGGCCGCA | AGCGCAAGCC | CCGCTTCTAA | GTCACCACGC | GGTTCTGGAA | AGGCACTTGC | 900 |
| 55 | CTCTGCACTT | TTCTATATTG | TTCAGCTGAC | AAAGTAGTAT | TTTAGAAAAG | TTCTAAAGTT | 960 |
| | ATAAAAATGT | TTTCTGCAGT | AAAAAAAAG | TTCTCTGGGC | CGGGCGTGGT | GGCTCACACC | 1020 |
| 60 | TGTAATCCCA | GCACCTTGGG | AGGCTGAGGT | GGGAGGATCA | TTTGAGGCCA | GGAGTTTGAG | 1080 |

| | ACCTGCCTGG GCAACATAAT GAAACTTCCT TTCCAGGGAG AAAAAAAAAA | 1140 |
|----|--|------|
| | A | 1141 |
| 5 | | |
| | (2) INFORMATION FOR SEQ ID NO: 55: | |
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1560 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55: | |
| | TCCTTCTCTG GGGCGTCGC GTTGGCAGCG GATGCGGGAA GCCGGACTCT GGGCGTCATG | 60 |
| 20 | TACTACAAGT TTAGTGGCTT CACGCAGAAG TTGGCAGGAG CATGGGCTTC GGAGGCCTAT | 120 |
| | AGCCCGCAGA TINAAAGCCT GIGGTTTCCA CAGAAGCACC ACCTATCATA TITGCCACAC | 180 |
| 25 | CAACTAAACT GACCTCCGAT TCCACAGTGT ATGATTATGC TGGGAAAAAC AAAGTTCCAG | 240 |
| 23 | AGCTACAAAA GTTTTTCCAG AAAGCTGATG GTGTGCCCGT CTACCTGAAA CGAGGCCTGC | 300 |
| | CTGACCAAAT GCTTTACCGG ACCACCATGG CGCTGACTGT GGGAGGGACC ATCTACTGCC | 360 |
| 30 | TGATCGCCCT CTACATGGCT TCGCAGCCCA AAAACAAATG AGTTAGGCTG CAGAGGACTG | 420 |
| | GTTTGTTTTT TGGCATAAAC CCTTTGAAGT TCCTTTTTCA TTGTTAAATT AAAATTTTTT | 480 |
| 35 | TTTTTACTTG GATGGCTTAA CATTTTTGCA AGAAAAATAG GAAGATATGA AGATGATGTT | 540 |
| | TTGGTTTGTT TATGAAATGC ATATGGCTTG TCAGAGCTCA TTCGACAGTT AAAGCCATTG | 600 |
| | TTTAAAGAAA CGGTGCTTTG CTCTGTGTTT GTGCTCCTGA TTTCCCTGGA GGTTCTGGAT | 660 |
| 40 | GAAGGCTGAA CACAGGCTTG TTAATGTCAG TCTGTGCTGA GGACCTCAGG GACTTGAGGT | 720 |
| | TGCATTTTTG AGCATGGGGT GCAGGAGCCT TTCTGGATTT GGATGTGGCT ATGGAAAGAA | 780 |
| 45 | CACAGAAGCC AAGGTCATGT GCATGAAATG AGGAGTTTGA GTTAGTCACC TCGGGGATTT | 840 |
| | TTTCCATTTT GCAGTAAAAT GTTAAATTAA TGTAGCCTGC CTCTATTTGT TGGGCAGGTA | 900 |
| | ATTTCAAAGG GTTATTTGCC TCATCTCCTA TCTTTAGTGA AATCTTATGT GTAATTGTGT | 960 |
| 50 | GTATTTATTC CACCGTGGGA ACAGAGAATA CCTGTTTAGT GTTGCACTTT AGACTGGTGT | 1020 |
| | CTGTTTTGTT AATGCAGCTG TGCCACAAAT TCTCCTTTAT CTTTTAAAAA TGTTATAGCT | 1080 |
| 55 | TTAAATTTTG ATTTATTTTG ACTGTGGAAT AAATACATGA ATGAAAAATT TTAAGTTTGA | 1140 |
| | AGTTCTTTGA ATGACCTTTC AGAGTAATTT CAGAACACCA GCAGCATCTT AAACCTGAGT | 1200 |
| | CTAATTTCTT TCTTGTTAAT TAGGCACCAG ATAATCTTTA TAAAATGGTC TTAAAAGCTA | 1260 |
| 60 | CONTRACTOR CONTRACTOR ACCORDANCE ACCORDANCE CONTRACTOR OF THE CONT | 122 |

| | CCCCTWAGTG AAAGGTACCT GTAACYCACA GTYCATTTAG ACACTAATTT CCTYTGCYGT | 1380 |
|-----------|--|------|
| | CATGATTGGK AGACTTCACT TACCCTATAT TAATTTTGAA AAAAGGTGGA ATTTTATTAT | 1440 |
| 5 | ATATGAAGGA ATAGTTTGTA TCTTACCATA GCACAGAACA GTGACCTCTT GCTCAGGATA | 1500 |
| | AGATGTGGTG ATTTGAAAAT ACTCATAGTA GCCTTGCAGT GATACCTCTC TCNCTCTCTC | 1560 |
| 10 | | |
| | | |
| | (2) INFORMATION FOR SEQ ID NO: 56: | |
| 15 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1507 base pairs | |
| | (B) TYPE: nucleic acid (C) STRANDEDNESS: double | |
| 20 | (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56: | |
| | GGAACGCAGA GCGGAGCGTG GAGAGCGGAG CGAAGCTGGA TAACAGGGGA CCGATGATGT | 60 |
| 25 | GGCGACCATC AGTTCTGCTG CTTCTGTTGC TACTGAGGCA CGGGGCCCAG GGGAAGCCAT | 120 |
| | CCCCAGACGC AGGCCCTCAT GGCCAGGGGA GGGTGCACCA GGCGGCCCCC CTGAGCGACG | 180 |
| 20 | CTCCCCATGA TGACGCCCAC GGGAACTTCC AGTACGACCA TGAGGCTTTC CTGGGACGGG | 240 |
| 30 | AAGTGGCCAA GGAATTCGAC CAACTCACCC CAGAGGAAAG CCAGGCCCGT CTGGGGCGGA | 300 |
| | TCGTGGACCG CATGGACCGC GCGGGGGACG GCGACGCTG GCTGTCGCTG GCCGAGCTTC | 360 |
| 35 | GCGCGTGGAT CGCGCACACG CAGCAGCGGC ACATACGGGA CTCGGTGAGC GCGGCCTGGG | 420 |
| | ACACGTACGA CACGGACCGC GACGGGCGTG TGGGTTGGGA GGAGCTGCGC AACGCCACCT | 480 |
| 40 | ATGGCCACTA CGCGCCCGGT GAAGAATTTC ATGACGTGGA GGATGCAGAG ACCTACAAAA | 540 |
| 40 | AGATGCTGGC TCGGGACGAG CGGCGTTTCC GGGTGGCCGA CCAGGATGGG GACTCGATGG | 600 |
| | CCACTCGAGA GGAGCTGACA GCCTTCCTGC ACCCCGAGGA GTTCCCTCAC ATGCGGGACA | 660 |
| 45 | TCGTGATTGC TGAAACCCTG GAGGACCTGG ACAGAAACAA AGATGGCTAT GTCCAGGTGG | 720 |
| | AGGAGTACAT CGCGGATCTG TACTCAGCCG AGCCTGGGGA GGAGGAGCCG GCGTGGGTGC | 780 |
| 50 | AGACGGAGAG GCAGCAGTTC CGGGACTTCC GGGATCTGAA CAAGGATGGG CACCTGGATG | 840 |
| 50 | GGAGTGAGGT GGGCCACTGG GTGCTGCCCC CTGCCCAGGA CCAGCCCCTG GTGGAAGCCA | 900 |
| | ACCACCTGCT GCACGARAGC GACACGGACA AGGAYGGGCG GCTGAGCAAA GCGSAAATCC | 960 |
| 55 | TGGGTAATTG GAACATGTTT GTGGGCAGTC AGGCCACCAA CTATGGYGAG GACCTGACCC | 1020 |
| | GGCACCACGA TGAGCTGTGA GCMCCGNGCA CCTGCCACAG CCTCAGAGGC CCGCACAATG | 1080 |
| 60 | ACCGGAGGAG GGGCCGCTGT GGTCTGGCCC CCTCCCTGTC CAGGCCCCCGC AGGAGGCAGA | 1140 |
| 60 | | |

| | TGCAGTCCCA GGCATCCTCC TKCCCCTGGG CTCTCAGGGA CCCCCTGGGT CGGCTTCTGT | 1200 |
|----|--|------|
| | CCCTGTCACA CCCCCAACCC CAGGGAGGGG CTGTCATAGT CCCAGAGGAT AAGCAATACC | 1260 |
| 5 | TATTTCTGAC TGAGTCTCCC AGCCCAGACC CAGGGACCCT NGGCCCCAAG CTCAGCTCTA | 1320 |
| | AGAACCGCCC CAACCCCTCC AGCTCCAAAT CTGAGCCTCC ACCACATAGA CTGAAACTCC | 1380 |
| 10 | CCTGGCCCCA GCCCTCTCCT GCCTGGCCTG GCCTGGGACA CCTCCTCTCT GCCAGGAGGC | 1440 |
| 10 | AATAAAAGCC AGCGCCGGGA AAAAAAAAAA AAAAAAAAA AAAAAAAA | 1500 |
| | AAAAAAN | 1507 |
| 15 | | |
| | (2) INFORMATION FOR SEQ ID NO: 57: | |
| 20 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 450 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 25 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57: | |
| | GAATTCGGCA CGAGCAGTGT CCAACACTGT AGCTGGTGCC TGCCAGGTTC CCAGTGGCTG | 60 |
| 30 | GGGTCACCAG GTCTGAAGAG AGATGTGCTG GCTGCGGGCA TGGGSCCAGA TCYTCCTGCC | 120 |
| 50 | AGTTTTCYTC TCCYTCTTTC TCATCCAATT GCTTATCAGC TTCTCAGAGA ATGGTTTTAT | 180 |
| | CCACAGCCCC AGGAACAATC AGAAACCAAG AGATGGGAAT RAAGAGGAAT GTGCTGTAAA | 240 |
| 35 | GAAGAGTTGT CAATTGTGCA CAGAAGATAA GAAATATATG ATGAATAGAT AATTGAAAAG | 300 |
| | AGATCCTCCA GAAAGAGCAG AAGGAAGTTT CTTCAATGGC TTCCTTCAGG ATTTTAATCA | 360 |
| 40 | TCCTTACAGC CTCTTTGAGA ATGATTGAAC TTCCAAATTC CCTGAAGTTA AAATTTTAAA | 420 |
| | TTCTATTAAA CATTTTTTCG AGTAAAAAA | 450 |
| 45 | | |
| 45 | | |
| | (2) INFORMATION FOR SEQ ID NO: 58: | |
| 50 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1147 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 55 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58: | |
| | GGCACGAGAC CCATTGAGCA GAAGGAGGCC AGGTGGGAAA GCTCCTGGGA AGAGCAGCCA | 60 |
| 60 | GACTGGACAC TGGGCTGCTT GAGTCCTGAG TCACAATTCA GAATTCCTGG GCTCCCTGGG | 120 |

| | TGCATTCTAT | САПТССАСТТ | GAAAGTTTGC | TTCCTTCCAG | TCATGTGGCT | CTTCATTCTA | 180 |
|----|------------|------------|------------|------------|------------|------------|------|
| | | | | | | | 240 |
| | CTCTCCTTGG | CTCTCATTTC | AGATGCCATG | GTCATGGATG | AAAAGGTCAA | GAGAAGCTTT | 240 |
| .5 | GTGCTGGACA | CGGCTTCTGC | CATCTGCAAC | TACAATGCCC | ACTACAAGAA | TCACCCCAAA | 300 |
| | TACTGGTGCC | GAGGCTATTT | CCGTGACTAC | TGCAACATCA | TCGCCTTCTC | CCCTAACAGC | 360 |
| 10 | ACCAATCATG | TGGCCCTGAA | GGACACAGGG | AACCAGCTCA | TTGTCACTAT | GTCCTGCCTG | 420 |
| 10 | AACAAAGAAG | ACACGGGCTG | GTACTGGTGT | GGCATCCAGC | GGGACTTTGC | CAGGGATGAC | 480 |
| | ATGGATTTTA | CAGAGCTGAT | TGTAACTGAC | GACAAAGGAA | CCTGGCCAAT | GACTTTGGTC | 540 |
| 15 | TGGGAAAGAC | TATCAGGCAC | AAAACCAGAA | GCTGCAAGGC | TCCCAAAGTT | GTCCGCAAGG | 600 |
| | CTGACCGCTC | CAGGACGTCC | ATTCTCATCA | TTTGCATACT | GATCACGGGT | TTGGGAATCA | 660 |
| 20 | TCTCTGTAAT | CAGTCATTTG | ACCAAAAGGA | GGAGAAGTCA | AAGGAATAGA | AGGGTAGGCA | 720 |
| 20 | ACACTTTGAA | GCCCTTCTCG | CGTGTCCTGA | CTCCAAAGGA | AATGGCTCCT | ACTGAACAGA | 780 |
| | TGTGACTGAA | GATTTTTTA | ATTTAGTTCA | TAAAGTGATG | CTACAACAGA | ATAATCACCA | 840 |
| 25 | TGACAACTGG | CCCCACACCT | CAGAGACTGA | TTCTGATCTC | CCAGGAATTC | TGAAGGTCCC | 900 |
| | TCTATCCTTG | ACAACAATCA | TTTGCAGCCA | GGTAGCAACG | GCAGTAGTCA | GAGGAGCTAT | 960 |
| 30 | GATAGACCAC | ACCCAAGCAA | GGCTGCCCTC | AAATAACATC | TCAAGATCTT | AGTTCTTATG | 1020 |
| 30 | CATTCCATCA | GTCAGAAGTG | AAGAAGAGGT | GGAGAATCTG | GATTGGGGAC | CAGGAAATCA | 1080 |
| | CTTGTATTTT | GTTAGCCAAT | AAATTCCTAG | CCAGTGTTGA | ATGAAAAAA | ААААААААА | 1140 |
| 35 | АААААА | | | | | | 1147 |

40 (2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 777 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

GGCAGAGGCT CCTCAGAAGG GCGTGGGCTC TCCAGTCTC CACAGTCCCC ACCATGCCCT

GTTGCCTTAC CGCTGACGTA GCTCACCCAT CTTTTACTTG CCTGGCTAAG ATGCATGGCA

TYWCATTTCC TCCTTGTTGC ACTGCAGTCA GTCCCTCACT GCCCCCATCT CCTGGAAGAG

GAGCATAAGC TTTGCAAGGT CAGCCACTTC TCTGGGGTCA CACTAGTTAC ATCAAGACAG

GACTCCAGCT CATATGTGCC AGTGCAGACA CTCTTCATCC ACCTGGGGCC CTGGGCTTGG

GACCTGGYTC CTTGCACAGC AGARGACCCG GAGGCTGAGA GGAGCTTGCG GTTGTGTCAT

360

| | AGTCACCTGG | CCAGARGGAA | CGTGAGCCCC | TCCCAAGCTG | CAGARGGARG | GARCARGCGT | 420 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 5 | GGCTGTCAGC | ACCGAGGTAG | CAGAGAATTA | ACATTCTTGT | CAGCAGAGAA | TGAAGCAGGA | 480 |
| J | ATATAATTAA | AACTTTGCCC | TTGGAATAGC | TGATTCATTT | GAATTTTATT | CCACACGTTT | 540 |
| | GAAAGAGGAA | AGAAAATGTG | AAGACTTGCA | GCCTGGTTCT | CGCCTGGCCT | GGGCTGGCCC | 600 |
| 10 | AGCTGTCAGG | CCCGGTTCCT | TTCTGAGCAT | TCAGTCCACT | GATGTTGACT | GAGGCCAGG | 660 |
| | AGAGACCCTC | AGCAGGGTAT | TACCATATCA | GCCTCCTATC | GCTGCTGGGA | GAAATTACCA | 720 |
| 15 | TGAATTCAGT | GGCTTAAAAC | AACACACGAG | CCTCTCTGAG | CCTACCCTGG | CTCAGGA | 777 |
| 15 | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 60:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1191 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

AAGANIGATT TTCCTTACTC TCCAAAGCGT CAGCATTTTG AAGTTTCTTT TATGAAAGTG

GGGGCAAGAA TCAGGGTGAA AATGAGTGTA AACAAAGCCC ATCCTGTGGT CAGCACCCAC 120 TGGAGGTGGC CAGCAGAGTG GCCTCAGATG TTCCTGCACC TGGCCCAGGA GCCCAGGACA 180 240 GAGGTCAAAT CTAGGCCCCT TGGTCTGGCT GGATTCATCA GGCAAGATTC GAAAACAAGA AAACCTCTAG AACAAGAAAC AATCATGTCT GCAGCAGATA CGGCACTGTG GCCCTATGGC 300 360 CATGCCAATC GTGAGCACCA AGAGAATGAG TTACAGAAAT ATCTCCAATA CAAAGACATG CATCTCCTGG ACAGTGGACA GTCGCTGGGA CACACACA CACTTCAAGG CTCACACAAC 420 CTAACAGCCT TAAATATCTG AAGAAACAGA ATCACGACAT TAAGTCAGCA GAGGGAGAGG 480 TAGGCTGAAG CAGCAGGAGG CCAATTTTAT ATCCCACAGA TTTTTTTAAA AATGACTCCC 540 CAGCAAGGG TGGGGAGAAA GCCACTGATT TAGGAGAGTT CTTGGCTCAG CCAACCACTG 600 660 CGGTTATCTA CACGTTTTAC AAAGGCACRG AAGTAGAGAG GGGCTGCACT CACGACCCTC CCCAGGGCCC GCACAGCCAG ACACGGTGGG TTCTTCCTTT TTCCCTTCTG GCCTTGGTGG 720 AATTCCTACC ACGGTGGCCT CTGCCTTTGG GACAATGCCT TCATGCTCAT CCCCGGGTCA 780 AGGATGGAGT CTGTTACCAT TTTCCAGGGG AAATTCCAAG GACCAGCCCC GCCTCATTAC 840 GTTCACCCCA CAGGAAGGTG ATCTGGAAAG CCTGTAAACA CGTACTCTGG GTGGCTGAGT 900 GGTGTCACCA AGCTGCTTTT GTGCAGGGCT GAAGCACAGA CAAGAGGGCA GGCAGCTGCC 960

| | GGAGGCCTGA | AGTGGGGAGA | GATCCCCGCA | GGCCTGCAGG | AGCCAGGGAG | AACCTCCAAC | 1020 |
|---|------------|------------|------------|------------|------------|------------|------|
| | TGGATCTAAA | CTGTGGGACA | GCCCAGGCGT | GCCCCTCTTC | ACATGGCTCC | CAGGCTCCCT | 1080 |
| 5 | CAAAGCCCTT | CCCAGGCCCT | GCAGGAAGAG | AGGGAGGGTG | AGGAGAGGCA | GGGAGGCCAG | 1140 |
| | AGGTCGCCTG | AAAGCCTGGG | CTCCGAACTC | CCTCAGCAGA | GCTTTAAAGT | G | 1191 |

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(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1580 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

| | CCCCGCCCCC | CGCCCACGAA | GGAAGTGGCT | GCTGCTCCGG | CGCGGACCCA | GAGCCGGTTC | 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| 25 | GGCGCGTCGA | CTGCCCAGAG | TCCGCGGCCG | GGCGCGGGAG | GAGCCAAGCC | GCCATGGCCT | 120 |
| 23 | ACCACAGCTT | CCTGGTGGAG | CCCATCAGCT | GCCACGCCTG | GAACAAGGAC | CGCACCCAGA | 180 |
| | TIGCCATCTG | CCCCAACAAC | CATGAGGTGC | ATATCTATGA | AAAGAGCGGT | GCCAAATGGA | 240 |
| 30 | CCAAGGTGCA | CGAGCTCAAG | GAGCACAACG | GGCAGGTGAC | AGGCATCGAC | TGGGCCCCCG | 300 |
| | AGAGTAACCG | TATTGTGACC | TGCGGCACAG | ACCGCAACGC | CTACGTGTGG | ACGCTGAAGG | 360 |
| 35 | GCCGCACATG | GAAGCCCACG | CTGGTCATCC | TGCGGATCAA | CCGGGCTGCC | CGCTGCGTGC | 420 |
| 33 | GCTGGGCCCC | CAACGAGAAC | AAGTTTGCTG | TGGGCAGCGG | CTCTCGTGTG | ATCTCCATCT | 480 |
| | GTTATTTCGA | GCAGGAGAAT | GACTGGTGGG | TTTGCAAGCA | CATCAAGAAG | CCCATCCGCT | 540 |
| 40 | CCACCGTCCT | CAGCCTGGAC | TGGCACCCCA | ACAATGTGCT | GCTGGCTGCC | GGCTCCTGTG | 600 |
| | ACTTCAAGTG | TCGGATCTTT | TCAGCCTACA | TCAAGGAGGT | GGAGGAACGG | CCGGCACCCA | 660 |
| 45 | CCCCGTGGGG | CTCCAAGATG | CCCTTTGGGG | AACTGATGTT | CGAATCCAGC | AGTAGCTGCG | 720 |
| 43 | GCTGGGTACA | TGGCGTCTGT | TTCTCAGCCA | GCGGGAGCCG | CGTGGCCTGG | GTAAGCCACG | 780 |
| | ACAGCACCGT | CTGCCTGGCT | GATGCCGACA | AGAAGATGGC | CGTCGCGACT | CTGGCCTCTG | 840 |
| 50 | AAACACTACC | ACTGCTGGCG | CTGACCTTCA | TCACAGACAA | CAGCCTGGTG | GCAGCGGGCC | 900 |
| | ACGACTGCTT | CCCGGTGCTG | TTCACCTATG | ACGCCGCCGC | GGGGATGCTG | AGCTTCGGCG | 960 |
| 55 | GGCGGCTGGA | CGTTCCTAAG | CAGAGCTCGC | AGCGTGGCTT | GACGGCCCGC | GAGCGCTTCC | 1020 |
| 33 | AGAACCTGGA | CAAGAAGGCG | AGCTCCGAGG | GTGGCACGGC | TGCGGGGGGG | GGCCTAGACT | 1080 |
| | CGCTGCACAA | GAACAGCGTC | AGCCAGATCT | CGGTGCTCAG | CGGCGGCAAG | GCCAAGTGCT | 1140 |
| 60 | CGCAGTTCTG | CACCACTGGC | ATGGATGGCG | GCATGAGTAT | CTGGGATGTG | AAGAGCTTGG | 1200 |

| | AGTCAGCCTT GAAGGACCTC AAGATCAAAT GACCTGTGAG GAATATGTTG CCTTCATCCT | 1260 |
|------------|--|------|
| 5 | AGCTGCTGGG GAAGCGGGGA GAGGGGTCAG GGAGGCTAAT GGTTGCTTTG CTGAATGTTT | 1320 |
| <i>3</i> . | CTGGGGTACC AATACGAGTT CCCATAGGGG CTGCTCCCTC AAAAAGGGAG GGGACAGATG | 1380 |
| | GGGAGCTTTT CTTACCTATT CAAGGAATAC GTGCCTTTTT CTTAAATGCT TTCATTTATT | 1440 |
| 10 | GAAAAAAAA AAAAATGCCC CCAAAGCACT ATGCTGGTCA TGAACTGCTT CAAAATGTGG | 1500 |
| | AGGTAATAAA ATGCAACTGT GTAAAAAAAA AAAAAAAAA AAATGACCCT CGCGATCTAG | 1560 |
| 15 | AACTAGNCGG ACGCNTGGGT | 1580 |
| 20 | (2) INFORMATION FOR SEQ ID NO: 62: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1117 base pairs (B) TYPE: nucleic acid | |
| 25 | (C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62: | |
| | GGCACGAGGC GCGATGCAGC ACAGGCTAGA GGCTGCGCAA SGCGGGGGCC CGCCCCTGGG | 60 |
| 30 | ACCCTCCGGG CCGGGCGGTT TGGCCCCTTA GCGCCCGGGC GTCGGGGCGG TAAAAGGCCG | 120 |
| | GCAGAAGGGA GGCACTTGAG AAATGTCTTT CCTCCAGGAC CCAAGTTTCT TCACCATGGG | 180 |
| 35 | GATGTGGTCC ATTGGTGCAG GAGCCCTGGG GGCTGCTGCC TTGGCATTGC TGCTTGCCAA | 240 |
| | CACAGACGTG TTTCTGTCCA AGCCCCAGAA AGCGGCCCTG GAGTACCTGG AGGATATAGA | 300 |
| 40 | CCTGAAAACA CTGGAGAAGG AACCAAGGAC TTTCAAAGCA AAGGAGCTAT GGGAAAAAAA | 360 |
| 40 | TGGAGCTGTG ATTATGGCCG TGCGGAGGCC AGGCTGTTTC CTCTGTCGAG AGGAAGCTGC | 420 |
| | GGATCTGTCC TCCCTGAAAA GCATGTTGGA CCAGCTGGGC GTCCCCCTCT ATGCAGTGGT | 480 |
| 45 | AAAGGAGCAC ATCAGGACTG AAGTGAAGGA TTTCCAGCCT TATTTCAAAG GAGAAATCTT | 540 |
| | CCTGGATGAA AAGAAAAGT TCTATGGTCC ACAAAGGCGG AAGATGATGT TTATGGGATT | 600 |
| 50 | TATCCGTCTG GGAGTGTGGT ACAACTTCTT CCGAGCCTGG AACGGAGGCT TCTCTGGAAA | 660 |
| 30 | CCTGGAAGGA GAAGGCTTCA TCCTTGGGGG AGTTTTCGTG GTGGGATCAG GAAAGCAGGG | 720 |
| | CATTCTTCTT GAGCACCGAG AAAAAGAATT TGGAGACAAA GTAAACCTAC TTTCTGTTCT | 780 |
| 55 | GGAAGCTGCT AAGATGATCA AACCACAGAC TTTGGCCTCA GAGAAAAAAT GATTGTGTGA | 840 |
| | AACTGCCCAG CTCAGGGATA ACCAGGGACA TTCACCTGTG TTCATGGGAT GTATTGTTTC | 900 |
| 60 | CACTCGTGTC CCTAAGGAGT GAGAAACCCA TTTATACTCT ACTCTCAGTA TGGATTATTA | 960 |
| | | |

| | ATGTATTTTA ATATTCTGTT TAGGCCCACT AAGGCAAAAT AGCCCCAAAA CAAGACTGAC | 1020 |
|----|--|------|
| | AAAAATCTGA AAAACTAATG AGGATTATTA AGCTAAAACC TGGGAAATAG GAGGCTTWAA | 1080 |
| 5 | ATGACTGCCM GCTGGTGCRT GCTCACACTT GGCCCAC | 1117 |
| | | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 63: | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 361 base pairs | |
| 15 | (B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63: | |
| 20 | CCCACGCGTG CKGGCGCCTG GCAGCCACCG CCTGGGAGGT TACTGTAAGG CCCGCAGCTC | 60 |
| 20 | CCGCCAGCTC CCGCGGACTS CTGCCGCCTC CTTACCATGA AGCCAGTAAG TCGTCGCACG | 120 |
| | CTGGACTGGA TTTATTCAGT GTTGCTGCTT GCCATCGTTT TAATCTCCTG GGGCTGCATC | 180 |
| 25 | ATCTATGCTT CGATGGTGTC TGCAAGACGA CAGCTAAGGA AGAAATACCC AGACAAAATC | 240 |
| | TTTGGGACGA ATGAAAATTT GTAACTCTTC TGGATTTAAT TATCTGAAAA TACAGTTCTT | 300 |
| 30 | TCCCTCATGC TTATGTAGAT ATAAAAATAA AATTCATAAT GCAAAAAAAA AAAAAAAAA | 360 |
| 30 | | 361 |
| | G | 361 |
| 35 | | |
| | (2) INFORMATION FOR SEQ ID NO: 64: | |
| 40 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1668 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 45 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64: | |
| | GGCACGAGGT CTGCCAAGCT ATAGACCATG GCTGTGAACA CATTTGTGTG AACAGTGACG | 60 |
| 50 | ACTCATACAC GTGCGAGTGC TTGGAGGGAT TCCGGCTCGC TGAGGATGGG AAACGCTGCC | 120 |
| 50 | GAAGAAGGAT GTCTGCAAAT CAACCCACCA TGGCTGCGAA CACATTTGTG TTAATAATGG | 180 |
| | GAATTCCTAC ATCTGCAAAT GCTCAKAGGG ATTTGTTCTA GCTGAGGACG GAAGACGGTG | 240 |
| 55 | CAAGAAATGC ACTGAAGGCC CAATTGACCT GGTCTTTGTG ATCGATGGAT CCAAGAGTCT | 300 |
| | TGGAGAAGAG AATTTTGAGG TCGTGAAGCA GTTTGTCACT GGAATTATAG ATTCCTTGAC | 360 |
| 60 | AATTTCCCCC AAAGCCGCTC GAGTGGGGCT GCTCCAGTAT TCCACACAGG TCCACACAGA | 420 |
| / | | |

| | GTTCACTCTG | AGAAACTTCA | ACTCAGCCAA | AGACATGAAA | AAAGCCGTGG | CCCACATGAA | 480 |
|----|------------|------------|------------|------------|------------|------------|------|
| | ATACATGGGA | AAGGCTCTA | TGACTGGGCT | GGCCCTGAAA | CACATGTTTG | AGAGAAGTTT | 540 |
| 5 | TACCCAAGGA | GAAGGGCCA | GCCCTTTCC | ACAAGGGTGC | CCAGAGCAGC | CATTGTGTTC | 600 |
| | ACCGACGGAC | GGGCTCAGGA | TGACGTCTCC | GAGTGGGCCA | GTAAAGCCAA | GGCCAATGGT | 660 |
| 10 | ATCACTATGT | ATGCTGTTGG | GGTAGGAAAA | GCCATTGAGG | AGGAACTACA | AGAGATTGCC | 720 |
| 10 | TCTGAGCCCA | CAAACAAGCA | TCTCTTCTAT | GCCGAAGACT | TCAGCACAAT | GGATGAGATA | 780 |
| | AGTGAAAAAC | TCAAGAAAGG | CATCTGTGAA | GCTCTAGAAG | ACTCCGATGG | AAGACAGGAC | 840 |
| 15 | TCTCCAGCAG | GGGAACTGCC | AAAAACGGTC | CAACAGCCAA | CAGTGCAACA | CAGATATCTG | 900 |
| | TTTGAAGAAG | ACAATCTTTT | ACGGTCTACA | CAAAAGCTTT | CCCATTCAAC | AAAACCTTCA | 960 |
| 20 | GGAAGCCCTT | TGGAAGAAAA | ACACGATCAA | TGCAAATGTG | AAAACCTTAT | AATGTTCCAG | 1020 |
| 20 | AACCTTGCAA | ACGAAGAAGT | AAGAAAATTA | ACACAGCGCT | TAGAAGAAAT | GACACAGAGA | 1080 |
| | ATGGAAGCCC | TGGAAAATCG | CCTGAGATAC | AGATGAAGAT | TAGAAATCGC | GACACATTTG | 1140 |
| 25 | TAGTCATTGT | ATCACGGATT | ACAATGAACG | CAGTGCAGAG | CCCCAAAGCT | CAGGCTATTG | 1200 |
| | TTAAATCAAT | AATGTTGTGA | AGTAAAACAA | TCAGTACTGA | GAAACCTGGT | TTGCCACAGA | 1260 |
| 30 | ACAAAGACAA | GAAGTATACA | CTAACTTGTA | TAAATTTATC | TAGGAAAAA | ATCCTTCAGA | 1320 |
| 30 | ATTCTAAGAT | GAATTTACCA | GGTGAGAATG | AATAAGCTAT | GCAAGGTATT | TTGTAATATA | 1380 |
| | CTGTGGACAC | AACTTGCTTC | TGCCTCATCC | TGCCTTAGTG | TGCAATCTCA | TTTGACTATA | 1440 |
| 35 | CGATAAAGTT | TGCACAGTCT | TACTTCTGTA | GAACACTGGC | CATAGGAAAT | GCTGTTTTTT | 1500 |
| | TGTAYTGGAC | TTTACCTTGA | TATATGTATA | TGGATGTATG | CATAAAATCA | TAGGACATAT | 1560 |
| 40 | GTACTTGTGG | AACAAGTTGG | ATTTTTTATA | CAATATTAAA | ATTCACCACT | TCAGAGRAAA | 1620 |
| .0 | ААААААААА | AAAAAAAA | АААААААА | AAAAAAAA | AAANAAA | | 1668 |

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(2) INFORMATION FOR SEQ ID NO: 65:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1353 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

GGGTCGACCC ACGCGTCCGC CCACGCGTCC GGATGGCTGC GCTGTTGCTG AGACACGTTG 60
GTCGTCATTG CCTCCGAGCC CACTTTAGCC CTCAGCTCTG TATCAGAAAT GCTGTTCCTT 120

TGGGAACCAC GGCCAAAGAA GAGATGGAGC GGTTCTGGAA TAAGAATATA GGTTCAAACC 180

| | GTCCTCTGTC | TCCCCACATT | ACTATCTACA | GTTGGTCTCT | TCCCATGGCG | ATGTCCATCT | 240 |
|--|------------|--------------|-------------|------------|------------|------------|------|
| ~ | GCCACCGTGG | CACTGGTATT | GCTTTGAGTG | CAGGGGTCTC | TCTTTTTGGC | ATGTCGGCCC | 300 |
| 5 TO C. 10 A' A' A' C. 15 TO C | TGTTACTCCC | TGGGAACTTT | GAGTCTTATT | TGGAACTTGT | GAAGTCCCTG | TGTCTGGGGC | 360 |
| | CAGCACTGAT | CCACACAGCT | AAGTTTGCAC | TTGTCTTCCC | TCTCATGTAT | CATACCTGGA | 420 |
| 10 | ATGGGATCCG | ACACTTGATG | TGGGACCTAG | GAAAAGGCCT | GAAGATTCCC | CAGCTATACC | 480 |
| | AGTCTGGAGT | GGTTGTCCTG | GTTCTTACTG | TGTTGTCCTC | TATGGGGCTG | GCAGCCATGT | 540 |
| | GAAGAAAGGA | GGCTCCCAGC | ATCATCTTCC | TACACATTAT | TACATTCACC | CATCTTTCTG | 600 |
| 15 | TTTGTCATTC | TTATCTCCAG | CCTGGGAAAA | GTTCTCCTTA | TTTGTTTAGA | TCCTTTTGTA | 660 |
| | TTTTCAGATC | TCCTTGGAGC | AGTAGAGTAC | CTGGTAGACC | ATAATAGTGG | AAAAGGGTCT | 720 |
| 20 | AGTTTTCCCC | TTGTTTCTAA | AGATGAGGTG | GCTGCAAAAA | CTCCCCTTTT | TTGCCCACAG | 780 |
| | CTTGCCTACT | CTCGGCCTAG | AAGCAGTTAT | TCTCTCTCCA | TATTGGGCTT | TGATTTGTGC | 840 |
| | TGAGGGTCAG | CTTTTGGCTC | CTTCTTCCTG | AGACAGTGGA | AACAATGCCA | GCTCTGTGGC | 900 |
| 25 | TTCTGCCCTG | GGGATGGGCC | GGGTTGGGGG | GTGGGTTGGT | GAGGCTTTGG | GTGCCACTGC | 960 |
| | CTGTGGGTTG | CTGGCTTAAA | GGACAATTCT | CTTCATTGGT | GAGAGCCCAG | GCCATTAACA | 1020 |
| 30 | CCTACACAGT | GTTATTGAAA | GAAGAGAGGT | GGGGTGGAG | GGGAATTAGT | CTGTCCCAGC | 1080 |
| | TAGAGGGAGA | TAAAGAGGC | TAGTTAGTTC | TTGGAGCAGC | TGCTTTTGAG | GAGAAAATAT | 1140 |
| | ATAGCTTTGG | ACACGAGGAA | GATCTAGAAA | ATTATCATTG | AACATATTAA | TGGTTATTTC | 1200 |
| 35 | TTTTTCTTGG | ATTTCCAGAA | AAGCCTCTTA | ATTTTATGCT | TTCTCATCGA | AGTAATGTAC | 1260 |
| | CCTTTTTTC | TGAAACTGAA | ттааатастс | ATTTTATCTT | TGAAAAAAA | AAAAAAAACC | 1320 |
| 40 | | CCCCGGACCC | | | | | 1353 |
| | | | | | | | |
| | | | | | | | |
| 45 | (2) INFORM | MATION FOR S | EQ ID NO: 6 | 6: | | | |

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1011 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

55 CGGAAGAAG CAGCCATCCA GACATTTCAG AACACGTACC AGGTGTTAGC TGTGACCTTC 60

AATGACACAA GTGATCAGAT TATTTCTGGT GGAATAGACA ATGATATCAA GGTCTGGGAC 120

TGCGCCAGAA CAAGCTAACC TACACCATGA GAGGCCATGC AGATTCAGTG ACTGGCCTGA 180

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| | GTTTAAGTTC | TGAAGGCTCT | TATCTTTTGT | CCAATGCAAT | GGACAATACA | GTTCGTGTCT | 240 |
|----|------------|------------|------------|------------|------------|-------------|------|
| | GGGATGTCCG | GCCATTTGCC | CCCAAAGAGA | GATGTGTAAA | GATATTTCAA | GGAAATGTGC | 300 |
| 5 | ACAACTTTGA | AAAGAACCTT | CTGAGATGTT | CTTGGTCACC | TGATGGAAGC | AAAATAGCAG | 360 |
| | CTGGCTCAGC | CGACAGGTTT | GTTTATGTGT | GGGATACCAC | AAGCAGGAGA | ATATTGTATA | 420 |
| 10 | AGCTGCCCGG | CCATGCTGGC | TCCATCAATG | AAGTGGCTTT | CCACCCTGAT | GAGCCCATCA | 480 |
| 10 | TTATCTCAGC | ATCGAGTGAC | AAGAGACTGT | ATATGGGAGA | GATTCAGTGA | AGATATGGAC | 540 |
| | TGGAAGACTC | CAAGGCCGCT | TGTCTTTGAG | ACCTCAGACT | GCATAAGTGA | TGCCAAATGT | 600 |
| 15 | TGGATGTCCA | GGYTAGCACC | CTCCCTTCAG | ATGACCATTG | CTAGCAAGAA | ACAGGAGGCG | 660 |
| | GTGGCCATAT | TCCAAAAACC | ACTTCTGTCC | CATTTCACCA | GGATGACTAA | GGCAAGCTCC | 720 |
| 20 | CTGTGGCCTC | TAAAAACCAC | CTGCCAGATT | TCAGGGACTG | TTTTTTTT | TCTTTTTCTT | 780 |
| 20 | TTTTCCTGTT | TTCTAATGCA | GGCCCAATGT | GACAAATTTG | TTGGTTGGGA | TALATALATAL | 840 |
| | TTTTTGTAAC | TGGCTTGTAT | GATATTTTCT | TTCTGTATTT | CTCTATATCA | TTTTGTATTA | 900 |
| 25 | AAAGCCAAAT | AGATGCCTTT | TTACAAGARM | АААААААА | AAAAAAAA | NNAAAAAAA | 960 |
| | CTGGGAGGG | GGGCCCGGTA | CCCAAATCGC | CGGATATGAT | CGTAAACAAT | С | 1011 |

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(2) INFORMATION FOR SEQ ID NO: 67:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1193 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

GGCCGGGCGG TGCGCACTGC GGGCGCATCC CTGCCCCGGC GCCGTCCGTG CCCGCGGGAC 60 CTGACAGCCG GGTCAGAGGG CGAACTGTGC TCAGGCCCGG GCTGGACGCA GAGCCAGAGC 120 TGTCCCCAGA GGAGCAGAGG GTCCTGGAAA GGAAGCTGAA AAAGGAACGG AAGAAAGAG 180 AGAGGCAGCG TCTGCGGGAG GCAGGCCTTG TGGCCCAGCA CCCGCCTGCC AGGCGCTCGG 240 GGGCCGAACT GGCCTGGGAC TACCTCTGCA GATGGGCCCA AAAGCACAAG AACTGGAGGT 300 TTCAGAAGAC GAGGCAGACG TGCCTCCTGC TGCACATGTA TGACAGTGAC AAGGTTCCCG 360 ATGAGCACTT CTCCACCCTG CTGGCCTACC TGGAGGGGCT GCAGGGCCGG GCCCGAGAGC 420 TGACGGTGCA GAAGGCGGAA GCCTGATGCG GGAGCTGGAT GAGGAGGGCT CTGATCCCCC 480 CCTGCCGGG AGGCCCAGC GCATCCGACA GNTGCTGCAG CTGCTCTCCT AGTGGGTTCA 540 600 GCGCGGGGG GGGCCGCTGC CCAGTGCAGG GCTGCCTCAG ACCACAGG GTGCAGCTCC

| | TCCGGCGGTG | GGGCCGGGT | TCACCAGCAG | GGCAGCGGCT | GAGCAAGGGC | TTTCAGCTCC | 660 |
|-----|------------|------------|------------|------------|------------|------------|------|
| _ | TCCGGTGGTG | GGGGCCGGGA | TCACCAGCAC | CAGAGCCTCG | CAAGGCCCC | TTCCCTCCTC | 720 |
| 5 | CAGACCCTCC | TTGGCCGGTG | ACGCTGTGAC | AGTGATGGCA | GGTTCAGTGC | CTTCAGCGCA | 780 |
| | GAGCGTGGAT | GCTCTGGAAT | CACCCGGACC | CCTGGCCTTG | GAGGGACCCT | CCAGCCCCAG | 840 |
| 10 | GAATCTGCTT | TGGAGGGAAA | TGTCTATTTT | TCTACCGGGA | ATATTTTAGA | GATTGGGGCA | 900 |
| | TGCTGGCTCC | TCCCGCCAGC | TGCAAACCTG | CACCTTCCGC | CTGATTCCCG | ATCCCCCTGC | 960 |
| 1.5 | GTGGGCCGCA | TTCCTGGTCC | CCTGCCTGCG | TCCATCGAGG | GGCCTGGCTG | TGGCCTGTTT | 1020 |
| 15 | TCCTTTGACC | CCACACAGCG | TCATTGCGGG | TCATGGGGAG | CCCCTGGTGG | GAGCTTGTGG | 1080 |
| | AGTCGGATCA | CGTACCTGTG | CAGAAACCGC | CTCTGTGGCT | GCATTTGAAA | TAAAACCCGA | 1140 |
| 20 | CCCAGCAGCA | ААААААААА | AAAAAANCNC | NAGGGGGGC | CCGGNACCCA | ATT | 1193 |
| | | | | | | | |

25 (2) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 560 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

| GAATTCGGCA | CGAGTTGGCA | CATGATGCAA | AATGCATTTC | TCAGAGTAGA | TTGCAGTCAA | 60 |
|------------|------------|------------|------------|------------|------------|-----|
| AAATGTTGGA | AACTACTAAG | CATGTGCARA | TAGCATGCAT | GCTGCTGCTG | ACCTGCCAGA | 120 |
| TATTTCTCCC | TTCCTCCCTT | TCTCCCTCAT | TTATTCATTC | ATTAACTGAT | TCATTCATCC | 180 |
| САТТАААААА | ATTATATGTA | TGTTTTGTGC | AAAGCACCCT | ACTCAAGGCT | GCGGGGTACA | 240 |
| AAAGTATATC | AGAAGCCTTG | GGCTTTGACM | WACTTCTCTG | TAGTAGTGCT | AGATTTGTGT | 300 |
| GGATCTGCCA | CACTTACTCC | AGGCCTCTTG | TGACCTGTGC | TTTGCATTAA | TCTCTTAGGC | 360 |
| TAAGCCACAT | ACCTTTTCAT | TATACAATCT | TTGCTGATGC | TAAGGACAGA | TTCCAAAGTG | 420 |
| CCCTCCTTAT | AATTTTTGTA | TTTAATGCAA | AGTGTAATCA | AGAATAGGCC | ATTGTTAGGT | 480 |
| CAATTGCTTT | TCTGTATTTA | TCTTTTCAAA | СААТАААТАА | TCAGTGGGAT | GAAAAAGGGC | 540 |
| CGGAAAAAA | АААААААА | | | | | 560 |

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(2) INFORMATION FOR SEQ ID NO: 69:

(i) SEQUENCE CHARACTERISTICS:

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(A) LENGTH: 1657 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

| | CGGACNGAGC | CGCCGCCGGG | CACTTCCTGT | GGAGGCCGCA | GCGGGTGCGG | GCGCCGACGG | 60 |
|----|------------|------------|------------|------------|---------------------|------------|------|
| 10 | GCGAGAGCCA | GCGAGCGAGC | GAGCGAGCCG | AGCCGAGCCT | CCCGCCGTCG | CCATGGGCCA | 120 |
| | GAACGACCTG | ATGGGCACGG | CCGAGGACTT | CGCCGACCAG | TTCCTCCGTG | TCACAAAGCA | 180 |
| 15 | GTACCTGCCC | CACGTGGCGC | GCCTCTGTCT | GATCAGCACC | TTCCTGGAGG | ACGCCATCCG | 240 |
| 13 | TATGTGGTTC | CAGTGGAGCG | AGCAGCGCGA | CTACATCGAC | ACCACCTGGA | ACTGCGGCTA | 300 |
| | CCTGCTGGCC | TCGTCCTTCG | TCTTCCTCAA | CTTGCTGGGA | CANTGACTGG | CTGCGTCCTG | 360 |
| 20 | GTGTTGAGCA | GGAACTTCGT | GCAGTACGCC | TGCTTCGGGC | TCTTTGGAAT | CATAGCTCTG | 420 |
| | CAGACGATTG | CCTACAGCAT | TTTATGGGAC | TTGAAGTTTT | TGATGAGGAA | CCTGGCCCTG | 480 |
| 25 | GGAGGAGGCC | TGTTGCTGCT | CCTAGCAGAA | TCCCGTTCTG | AAGGGAAGAG | CATGTTTGCG | 540 |
| | GGCGTCCCCA | CCATGCGTGA | GAGCTCCCCC | AAACAGTACA | TGCAGCTCGG | AGGCAGGGTC | 600 |
| | TTGCTGGTTC | TGATGTTCAT | GACCCTCCTT | CACTTTGACG | CCAGCTTCTT | TTCTATTGTC | 660 |
| 30 | CAGAACATCG | TGGGGCACAG | CTCTGATGAT | TTTAGTGGCC | ATTGG TTTT A | AAACCAAGCT | 720 |
| | GGCTGCTTIG | ACTCTTGTTG | TGTGGCTCTT | TGCCATCAAC | GTATATTTCA | ACGCCTTCTG | 780 |
| 35 | GACCATTCCA | GTCTACAAGC | CCATGCATGA | CTTCCTGAAA | TACGACTTCT | TCCAGACCAT | 840 |
| | GTCGGTGATT | GGGGGCTTGC | TCCTGGTGGT | GCCCTGGGC | CCTGGGGGTG | TCTCCATGGA | 900 |
| | TGAGAAGAAG | AAGGAGTGGT | AACAGTCACA | GATCCCTACC | TGCCTGGCTA | AGACCCGTGG | 960 |
| 40 | CCGTCAAGGA | CTGGTTCGGG | GTGGATTCAA | CAAAACTGCC | AGCTTTTATG | TATCCTCTTC | 1020 |
| | CCTTCCCCTC | CCTTGGTAAA | GGCACAGATG | TTTTGAGAAC | TTTATTTGCA | GAGACACCTG | 1080 |
| 45 | AGAATCAATG | GCTTCAGGAC | ATGGGTTCTC | TTCTCCTGTG | ATCATTCAAG | TGCTCACTGC | 1140 |
| | ATGAAGACTG | GCTTGTCTCA | GTGTTTCAAC | CTCACCAGGG | CTGTCTCTTG | GTCCACACCT | 1200 |
| | CGCTCCCTGT | TAGTGCCGTA | TGACAGCCCC | CATCAAATGA | CCTTGGCCAA | GTCACGGTTT | 1260 |
| 50 | CTCTGTGGTC | AAGGTTGGTT | GGCTGATTGG | TGGAAAGTAG | GGTGGACCAA | AGGAGGCCAC | 1320 |
| | GTGAGCAGTC | AGCACCAGTT | CTGCACCAGC | AGCGCCTCCG | TCCTAGTGGG | TGTTCCTGTT | 1380 |
| 55 | TCTCCTGGCC | CTGGGTGGGC | TAGGGCCTGA | TTCGGGAAGA | TGCCTTTGCA | GGGAGGGGAG | 1440 |
| | GATAAGTGGG | ATCTACCAAT | TGATTCTGGC | AAAACAATTT | CTAAGATTIT | TTTGCTTTAT | 1500 |
| | GTGGGAAACA | GATCTAAATC | TCATTTATG | CTGTATTTTA | TATCTTAGTT | GTGTTTGAAA | 1560 |
| 60 | ACGTTTTGAT | TTTTGGAAAC | ACATCAAAAT | AAATAATGGC | GTTTGTTGTA | ААААААААА | 1620 |

| | AAAAAAACTC GRGGGGGGC CCGGTACCCA AATCGCC | 1657 |
|----|---|------|
| 5 | | |
| | (2) INFORMATION FOR SEQ ID NO: 70: | |
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 711 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70: | |
| | GGCACGAGCG AAGACCCTGT TCGGACCCTG CCCCGATTCC AGACTCAGGT AGATCGTCGG | 60 |
| 20 | CATACCCTCT ACCGTGGACA CCAGGCAGCC CTGGGGCTGA TGGAGAGAGA TCAGGTATCC | 120 |
| 20 | CCCAGGGAGT AGGGGCTACC TTGAGGGGAT GATAGACCTC CCCCACTCCC AGTGKKACTC | 180 |
| | TGGAAATATG AAGGAACTAG GGAGTGGAAG AGATTTCAGA GCTGGGGAGA GGAGTTCCTC | 240 |
| 25 | CCTTCAAAGC CAGCAACTGC CTTTGGGGAA TGTCGGGGGG TCTCTCCTTT CTCCTGCTTG | 300 |
| | TTTRAGGTGG TACACAGTCC CCCCTTCAMC TGGSGGGAAG CTGTNCCGGA CARACTCATC | 360 |
| 30 | TCAGCTTTCC CTTGGGGCAG GATCGGGGGC AGCAGCTCCA GCAGAAACAG CAGGATCTGG | 420 |
| 30 | AGCAGGAAGG CCTCGAGGCC ACACAGGGGC TGCTGGCCGG CGAGTGGGCC CCACCCCTCT | 480 |
| | GGRAGCTGGG CAGCCTCTTC CAGGCCTTCG TGAAGAGGGA GAGCCAGGCT TATGCGTAAG | 540 |
| 35 | CTTCATAGCT TCTGCTGGCC TGGGGTGGAC CCAGGACCCC TGGGGCCTGG GTGCCCTGAG | 600 |
| | TGGTGGTAAA GTGGAGCAAT CCCTTCACGC TCCTTGGCCA TGTTCTGAGC GGCCAGCTTG | 660 |
| 40 | GCCTTTGCCT TAATAAATGT GCTTTATTTT CAAAAAAAAA AAAAAAAAAC T | 711 |
| | | |
| 45 | (2) INFORMATION FOR SEQ ID NO: 71: | |
| | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 935 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double | |
| 50 | (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71: | |
| 55 | GGCACAGGGT GAAAGCCAGC TAAACCCCAA GTGGAGAAGT GAAAGACATG GTTGTTCCCA | 60 |
| | TAAGTTTATT GCTCACATTA TGAAAGAAGC CATAGTCATG AGTGAACCAC TCCCTAGGTT | 120 |
| | GATAAGGAAA CCAACACGGA AGATCTCTTT CTGGAAGAAG CAGCCAGCCT CGTGAAGGAG | 180 |
| 60 | CGGCCCAGCC GCCGGGCCCG AGGGTCGCCT TTTGTTCGGA GTGGCACGAT TGTCCGTTCC | 240 |

| | CAGACATTCT | CGCCTGGAGC | ACGAAGCCAG | TATGTTTGCA | GACTTTATCG | TAGTGACAGC | 300 |
|----|-------------|--------------|---------------------------|-------------|------------|------------|-----|
| 5 | GACAGTTCAA | CGCTGCCCCG | GAAGTCCCCC | TTTGTCCGAA | ATACTTTGGA | AAGACGAACC | 360 |
| 5 | CTTCGCTATA | AGCAGTCATG | CAGGTCTTCC | CTGGCTGAGC | TCATGGCCCG | CACCTCCCTG | 420 |
| | GACTTGGAGC | TGGATCTCCA | GGCGTCGAGA | ACACGGCAGA | GGCAGCTGAA | TGAGGAGCTC | 480 |
| 10 | TGCGCCCTCC | GTGAGCTGCG | GCAGCGGTTN | GGAGGACGCC | CAGCTCCGTG | GCCAGACTGA | 540 |
| | CCTCCCACCC | TGGGTGCTTC | GGGACGAGCG | GCTCCGTGGC | CTGCTGCGGG | AGCCGAGCGG | 600 |
| 15 | CAGACAAGAC | AGACCAAACT | TGACTACCGT | CATGAGCAGG | CGGCTGAGAA | GATGCTGAAG | 660 |
| | AAGGCCTCCA | AGGAGATCTA | CCAGCTGCGT | GGCAGAGCCA | CAAAGAGCCC | ATCCAAGTGC | 720 |
| | AGACCTTTAG | GGAGAAGATA | GCATTCTTCA | CAAGGCCAAG | GATCAACATA | CCTCCTCTCC | 780 |
| 20 | CAGCCGACGA | CGTCTGATGG | AGTGCATTGT | GCACATGAAG | TATTTATCCA | CCTGTTTTAT | 840 |
| | TTTCATGAAG | TTCTTAGACT | AGCTGAATTT | GTCTTTAAAA | TATTTGTGCA | AAGCTATTAA | 900 |
| 25 | TATACACATT | TTGTAAAAAA | АААААААА | AAACT | | | 935 |
| | | | | | | | |
| | (2) INFORMA | ATION FOR SE | EQ ID NO: 72 | 2: | | | |
| 30 | (i) | SEQUENCE CH | HARACTERIST: | ICS: | | | |
| | | | GTH: 504 ba E: nucleic | - | | | |
| 35 | | | ANDEDNESS: OLOGY: line | | | | |
| | (xi |) SEQUENCE I | DESCRIPTION | : SEQ ID NO | : 72: | | |
| 40 | GCAGGGGCGA | GGGGYTGGGG | ACCGCGGGGC | GGACGGGAGC | GAGTATGTCC | GCTCTGACTC | 60 |
| 40 | GGCTGGCGTC | TTTCGCTCGC | GTTGGAGGCC | GCCTTTTCAG | AAGCGGCTGC | GCACGGACTG | 120 |
| | CTGGAGATGG | TGGAGTCCGT | CATGCCGGTG | GTGGTGTGCA | CATTGAGCCC | CGGTATAGAC | 180 |
| 45 | AGTTCCCCCA | GCTGACCAGA | TCCCAGGTGT | TCCAGAGCGA | GTTCTTCAGC | GGACTCATGT | 240 |
| | GGTTCTGGAT | TCTCTGGCGC | TTTTGGCATG | ACTCAGAAGA | GGTGCTGGGT | CACTTTCCGT | 300 |
| 50 | ATCCTGATCC | TTCCCAGTGG | ACAGATGAAG | AATTAGGTAT | CCCTCCTGAT | GATGAAGACT | 360 |
| 50 | GAAGGTGTAG | ACTCAGCCTC | ACTCTGTACA | AGAGCCAGGT | GAGAATTTCA | AGGATTATCG | 420 |
| | ACTTCATATT | GCACATTAAA | GTTACAAATT | AAAGTGGCTT | GGTCAAGAAT | GARAAAAAA | 480 |
| 55 | ТТААААААА | GGGGGGGGC | CCCN | | | | 504 |
| | | | | | | | |

 $60\,$ (2) information for SEQ ID No: 73:

| 5 | (1) SEQUENCE CHARACTERISTICS: (A) LENGTH: 620 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
|----------|---|-----|
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73: | |
| 10 | GAATTCGGCA CGAGGAGGAG GGGAGGCGGG GTAAGTTTGG TGGGAAACTC TGTAATTTCC | 60 |
| | WITTITACTT TCACAGCAAT AGTGCAGAAT CCAGAATGGA TGTCCTCTTT GTAGCCATCT | 120 |
| 1.5 | TTGCTGTGCC ACTTATCCTG GGACAAGAAT ATGAGGATGA AGAAAGACTG GGAGAGGATG | 180 |
| 15 | AATATTATCA GGTGGTCTAT TATTATACAG TCACCCCCAG TTATGATGAC TTTAGTGCAG | 240 |
| | ATTTCACCAT TGATTACTCC ATATTTGAGT CAGAGGACAG GCTGAACAGG TTGGATAAGG | 300 |
| 20 | ACATAACAGA AGCAATAGAG ACTACCATTA GTCTTGAAAC AGCACGTGCA GACCATCCGA | 360 |
| | AGCCTGTAAC TGTGAAACCA GTAACAACGG AACCTCAGAG TCCAGATCTG AACGATGCCG | 420 |
| 25 | TGTCCAGTTT GCGAAGTCCT ATTCCCCTCC TCCTGTCGTG TGCCTTTGTT CAGGTGGGGA | 480 |
| 43 | TGTATTTCAT GTAGAAGGTG GAAGAAGGCT GCTATGACTC TTTGGATGGG AGTCTGGCAA | 540 |
| | GAGGAAATTG GAAGATAAAA TAAATAATAA GTGAAATAAA AAAAAAAA | 600 |
| 30 | GGGGGGCCC GGTACCCAAT | 620 |
| 35 40 | (2) INFORMATION FOR SEQ ID NO: 74: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 581 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74: | |
| 45 | ACAAGGTGTG TGTAAAGTTT ATGTTTGTAA ACTGAATTCT ATCTTAAATC CAAAAAGAAC | 60 |
| | TCGGGAGTAA TTCATTTTTG TAGCATAAAG ATCCCTAAGT TTTATTTTGA AATATCTGAT | 120 |
| 50 | TTTTACACGT TAAAAAATAA CAGGGCATCG AGAGGATTCC TAGGTGACAT CCAGACTCCT | 180 |
| 50 | TTAGCTTTGT GTGTGGGCA CCGGTTAGTC TGCTTCTCT TCCTTTCTTG CACTGCTTCA | 240 |
| | CACAGCCATG CCCTGCCAGC CCGGGCAGGT GCCTTCCTGT CAATGTACAT TTGGGCTTCT | 300 |
| 55 | GCTCATGCTG CCCTCCCTCC CCTCCCCTGC CTCCCAACCC CGCCCCTTTT GTTCCTCCAT | 360 |
| | GGAGTACTTC CATGGGTGTG CCTCCCCCAG CCAAGCCATA ATAGGTGGTT TCCCCTTCGC | 420 |
| 60 | TTCTGTAGCC CTTGCAGACA TCCTCTGTTT ACAGTAGGTG TTGACTTACT TCCCCTCTCC | 480 |

| | CCGSTAAAGC CATAAACTCC TTAAGGACAG GTAGCATTCT TAGTATCTTC GTTCTTCTCA | 540 |
|---------|--|------|
| | ATGACCAGTA GACCATTAAA CATGTAGCAA ACAAATGTGA A | 581 |
| 5 | | |
| | | |
| | (2) INFORMATION FOR SEQ ID NO: 75: | |
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1843 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75: | |
| | AAACCCAACN CCCTCCGGTC CCCNAAAGAA AGCCCAGCCC AAATCCCAAG CCGGCAGTGA | 60 |
| 20 | GCCCGCGAAC AAGGCCCTCA AGACGCCCAG NCGAACAAGC AGCCCCCAGG AGGCCCCGCA | 120 |
| 20 | AGAGAACTCC CTGGCGGCCC AAGCGGGCAG CTTCTGTGCG GCAGAACTCA GCCACCGAGA | 180 |
| | GCGCAGACAG CATCGAGATT TATGTCCCGG AGNCCCAGAC CAGGCTCTGA GACCATGCAG | 240 |
| 25 | GAGGAAAGAA ACGATTITAA ATCATTAAAA ACACAAAAAC TAAGTGCGAA CGGAACAGAG | 300 |
| | | 360 |
| 20 | TTTTCTCAAC CTTTGCTATG GTTATTCTGT CTAGAGACCC TGAGCCAACT TTCAAATTGA | |
| 30 | CGCATACAAG GGCTCACAAT TTGGCTTTTT TGGGTCCCTC CCAGCTTTAG GTTATGAAGA | 420 |
| | TTTTACTCAC AAAAAAATC AACAAAAATC ACGAAACTAG AAAACTTTTT TTTTCCTCTT | 480 |
| 35 | GCTGGCCGTG GTGGACTAGA TAGATGGACG TCGGCAACTC CCGGCCCAGC CTCCATACTG | 540 |
| | CGGTCTTTTT ACTCGTTCTA TCTGATGAGA ACTCACACTA GCTTGTTTAC AAGATGACGA | 600 |
| | CAGTCCAAGG GCAGCCTTGG GCACCTGCCA TGTCCCTCCT TTCCCCAGCT ATCCCCGCTC | 660 |
| 40 | TGACCTTGAT TTTCATTCTT ATGTTTTTCT CTTTTCCCTT CAGAGCTCAC ACAGTGGTCA | 720 |
| | CCATTGTGGC AAGCGGCTTT CTGGGTCTCA GCCCTCTCTG CGGTTGAGGG CCCAGAGGAC | 780 |
| 45 | AGAGAGATGG ACATGCGTCC CCTCCCTCCC CCCGCCAAGT GCTCACACAC AACCTCACGC | 840 |
| -,5 | GCACACACA ACACGCAGAT GGAGGCGCCT CACTGGGAGG TGCCCCGCCA GCCCTGGGCA | 900 |
| | GTGTCAGGCA GGACTCACTC ACCGCTGAGC AGATGAGAGA AGTTTTAGTC TTGGCGGGTG | 960 |
| 50 | GAAATGAGAC GAAGCCACAG TTATCACACT CCAGACTCCT GCCCTTTTAT TTTCTCCAGC | 1020 |
| | CCCTTCTTCC TTCAGCAAAA TCTAGGACTC CCGAGTGGCT TCCAGGGGGC CGTCAGTCCT | 1080 |
| <i></i> | CAGCCGCGCC TGTGTCCGGT GCCCGAGGGG CGGGCGGCGG TGTCTGTATG TATGTGTACA | 1140 |
| 55 | TATGCACATA GACCTTAGAG TGTATAGTTA ACAAACGCCC ATCTGCTCAC CCATGCCCAC | 1200 |
| | CCAGCGCCGC CGCCGCTGGC TCTCGGGGGCA CCTGGCAGGA GGCGGGTGTG TGAATAGCAT | 1260 |
| 60 | ATATTTTTAC ATGTACTATA TCTAGGTGTG TGTACAAGTG TGTGTAAAAA TATATACCTT | 1320 |

| | GTGTGTAAGC | AGCCCTTTTT | TTTTTTGGTC | TCCACCCCC | TCCCCCCCCC | CCGCACTCCT | 1380 |
|----|-------------|-------------|--------------|------------|------------|------------|------|
| 5 | AAGGGCCCAT | CTGCCCAGCC | TCTGAGTTTT | CTGTTCTATT | TTTTTTTTAA | CCCCAATTAT | 1440 |
| 5 | CCTTCTCTCT | CTCCTGCCCC | CGCATCCCAC | TCCCAGGGTG | TCACGAGCCC | TGAGCTGCAA | 1500 |
| | TGGCCCGGGC | CTGCAGGGCG | GGGTAGGGGA | GGGCARGGCT | SAGCCCCGAA | GCCAGCTCAG | 1560 |
| 10 | TACCTGAGGG | GCTGCTCTAT | GCTGTGTATG | CGCCTCTCTG | GCATCCGAGA | CATCCTCTTG | 1620 |
| | GTGGCGCTTG | CTNGCAGGGG | ACCCCCCCC | CGTCCCCAGG | TGAACCAAGG | GTCTGCTCCG | 1680 |
| 15 | GGGCCCATTT | CCAGCTTGGC | CGCCGTCTGT | GACCTTGGGC | AAGTCACTTG | ACCTCTGTGT | 1740 |
| 13 | GCCTCAACTT | CCTCCTCTGT | AAAACGGGGA | CAGTCCCTGC | CCCTCCCTAC | CTCACAGGCA | 1800 |
| | TGTTGTGAGA | ATAAATGAGG | TAACGTGTAA | АААААААА | AAT | | 1843 |
| 20 | | | | | | | |
| | (2) INTEGEM | ATTON FOR S | FO ID NO: 70 | s · | | | |
| | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 76:

25 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1441 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

| | TCGACCCACG | CGTCCGGCTC | CCCGAGCCCT | GCCAACCATG | GTGAACTTGG | GTCTGTCCCG | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 35 | GGTGGACGAC | GCCGTGGCTG | CCAAGCACCC | GGGACTCGGG | GAGTATGCCG | CATGCCAGTC | 120 |
| | ACACGCCTTC | ATGAAGGGCG | TTTTCACCTT | CGTCACAGGC | ACCGGCATGG | CCTTTGGCTT | 180 |
| 40 | GCAGATGTTC | ATTCAGAGGA | AGTTTCCATA | CCCTTTGCAG | TGGAGCCTCC | TAGTGGCCGT | 240 |
| 40 | GGTTGCAGGC | TCTGTGGTCA | GCTACGGGGT | GACGAGAGTG | GAGTCGGAGA | AATGCAACAA | 300 |
| | CCTCTGGCTC | TTCCTGGAGA | CCGGGCAGCT | CCCCAAAGAC | AGGAGCACAG | ATCAGAGAAG | 360 |
| 45 | CTAGGAGAGC | TCCAGCAGGG | GCACAGAGGA | TTGGGGGCAG | GAGGAGTCTG | GAACACAGCC | 420 |
| | TTCATGCCCC | CTGACCCCAG | GCCGACCCTC | CCCACACCCT | AGGGTACCCC | AGTCGTATCC | 480 |
| 50 | TCTGTCCGCA | TGTKTGGCCA | GGCCTGACAA | ACACCTGCAG | ATGGCTGCTG | CCCCAACCTG | 540 |
| 50 | GGACCTGCCC | AGRAGGTTGG | AGCAGAAAGG | GCTCTCCCTG | GGGTGGTGTT | TCTCCTCTAG | 600 |
| | GGTATTGGGA | TGCATGTTCT | GCACTGCCAG | CAGAGAGGGT | GTGTCTGGGG | GCCACCACCT | 660 |
| 55 | ATGGGACACG | GGGTCGAAGG | GGCCTGTACA | CTCTGTCATT | TCCTTTCTAG | CCCCTGCATC | 720 |
| | TCCAACAAGT | CCAAGGTGAC | AGCTGGTGCT | AGGGCGTGG | GGTTAATAAA | TGGCTTATCC | 780 |
| 60 | TTCTCTCCAC | CCAAGTTTCC | ACCTGACCAG | GTGAAAAACA | AATCAGAAGG | GTAAGATGAT | 840 |

226

| | GACAGGTCAC | ATGAAACCTT | TATTACĆCTA | CAGTTGATAT | ATGAGGATCA | CATGCAAGTT | 900 |
|----|------------|------------|------------|------------|------------|------------|------|
| | ACATACTGAG | GATGTACAGG | GAAGTTCCCA | GCGCTGAACC | CCAGAATTAG | ACGTTCGCAT | 960 |
| 5 | CAGCCCCGTA | GGCCACGTGG | ACACCACCAC | AGCCTCTCTG | TATGGGGGTC | TGCCTCTGTA | 1020 |
| | GCACTTGGCA | TGTAGGGGCA | GAGCAAAAGG | GGCCANGCTG | GCCAGAGCCT | GGCTGCTGGG | 1080 |
| 10 | NAGARGAGGG | ACTTGTGGGS | CACGCCACNT | GCCTATCATT | CCCCAYTCAT | CTATTAGCCA | 1140 |
| | AAGTCACTCC | CCAGAGGCAG | AGCTAGCCCG | TTGTAGCCGT | GTCTGTGTGG | AGGGAAAGCT | 1200 |
| | TCTGAGTGGG | CAAGCCTACA | CACAGCCCCG | AGCCCCAAGA | GGAGGAAGAG | GTGGAGACCA | 1260 |
| 15 | GACGGAACCT | CCACAAGTCC | ATCATGGTTA | CAGCTGGCTT | CCCCGCAGCA | CCGAAGACCC | 1320 |
| | ACAGCATNGG | CCCTGCTGCC | CCCGACCCAG | CTCAGCTGCC | ANGCCTCACC | TTGCCAGGAA | 1380 |
| 20 | TTGAAAGAAA | GTTATTGAGT | ACTAATTGGC | CTCAGAGTNA | CAGGAAGCTC | AAGTTAAAGT | 1440 |
| | G | | | | | | 1441 |
| | | | | | | | |
| | | | | | | | |

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(2) INFORMATION FOR SEQ ID NO: 77:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 910 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

GGCAGAGCTG GCCTTCGACT CGCTATGTCC ACTAACAATA TGTCGGACCC ACGGAGGCCG 60 AACAAAGTGC TGAGGTGAGG ACCCCAGCGT CGTGGGCACG GGTTCGGGTT GTGGGTGTGG 120 40 ATCGGGGCCC TGGGAAGCGC CTGTCTATCC CGGGGGCAGG ACCTGAGCGC CCCTGACCCT 180 CGAGCCTGTC GCAGGTACAA GCCCCCGCCG AGCGAATGTA ACCCGGCCTT GGACGACCCG 240 ACGCCGGACT ACATGAACCT GCTGGGCATG ATCTTCAGCA TGTGCGGCCT CATGCTTAAG 300 45 CTGAAGTGGT GTGCTTGGGT CGCTGTCTAC TGCTCCTTCA TCAGCTTTGC CAACTCTCGG 360 AGCTCGGAGG ACACGAAGCA AATGATGAGT AGCTTCATGT GAGACTTGCC CTACAGAACA 420 50 AGTGACTCTT GAGTAAGGGG TGGGGGGACC CCAGCCTGGC CATCCTAGAC TGACACCTCT 480 CTCCTGTCTT CATGCTGTCC ATCTCTGCCG TGGTGATGTC CTATCTGCAG AATCCTCAGC 540 CCATGACGCC CCCATGGTGA TACCAGCCTA GAAGGGTCAC ATTTTGGACC CTGTCTATCC 600 55 ACTAGGCCTG GGCTTTGGCT GCTAAACCTG CTGCCTTCAG CTGCCATCCT GGACTTCCCT 660 GAATGAGGCC GTCTCGGTGC CCCCAGCTGG ATAGAGGGAA CCTGGCCCTT TCCTAGGGAA 720 60 CACCCTAGGC TTACCCCTCC TGCCTCCCTT CCCCTGCCTG CTGCTGGGGG AGATGCTGTC 780

| | CATGTTTCTA GGGGTATTCA TTTGCTTTCT CGTTGAAACC TGTTGTTAAT AAAGTTTTTC | 840 |
|----|--|------|
| _ | ACTCTGAAAA AAAAAAAAA AAAAAAAAAC TYGRGGGGGG GCCCGGAACC CAATTCSCCG | 900 |
| 5 | GATAGTGAGT | 910 |
| | | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 78: | |
| 15 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 2776 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| 20 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78: | |
| 20 | TCGACCCACG CGTCCGGGCG GGCAGTGATG GCGGCTGGTG ATGGGGACGT GAAGCTAGGC | 60 |
| | ACCCTGGGGA GTGGCAGCGA GAGCAGCAAC GACGGCGGCA GCGAGAGTCC AGGCGACGCG | 120 |
| 25 | GGAGCGGCAG CGRAAGGGGG AGGCTGGGCG GCGGCGGCGT TGGCGCTTCT GACGGGGGC | 180 |
| | GGGGAAATGC TGCTGAACGT GGCGCTGGTG GCTCTGGTGC TGCTGGGGGC CTACCGGCTG | 240 |
| 30 | TGGGTGCGCT GGGGGGCG GGGTCTGGGG GCCGGGGCCG GGGCGGCGA GGAGAGCCCC | 300 |
| | GCCACCTCTC TGCCTCGCAT GAAGAAGCGG GACTTCAGCT TGGAGCAGCT GCGCCAGTAC | 360 |
| | GACGGCTCCC GCAACCCGCG CATCCTGCTC GCGGTCAATG GGAAAGTCTT CGACGTGACC | 420 |
| 35 | AAAGGCAGCA AGTTCTACGG CCCGGCGGGT CCATATGGAA TATTTGCTGG TAGGGATGCC | 480 |
| | TCCAGAGGAC TGGCCACATT TTGCCTAGAT AAAGATGCAC TTAGAGATGA ATATGATGAT | 540 |
| 40 | CTCTCAGATT TGAATGCAGT ACAAATGGAG AGTGTTCGAG AATGGGAAAT GCAGTTTAAA | 600 |
| | GAAAAATATG ATTATGTAGG CAGACTCCTA AAACCAGGAG AAGAACCATC AGAATATACA | 660 |
| | GATGAAGAAG ATACCAAGGA TCACAATAAA CAGGATTGAA CTTTGTAAAC AACCAAAGTC | 720 |
| 45 | AGGGGCCTTC AGAACTGCAA TICTTACTCC CTTTCACAGA CTGTCCGGAG TCTTTGGGTT | 780 |
| | TGATTCACCT GCTGCGAAAA ACATTCAACA AATTGTGTAC AAGATAAATT AATCTCACTA | 840 |
| 50 | TGAAGATTTG AATAACTAGA CATTATTTAT GCTGCCAAAC TCATTTGTTG CAGTTGTTTG | 900 |
| | TAATGTCTAG TGGGGCTTCA TCATCCTGAA AAGAAGGAGA CAGGGATTTT TTTAAAGAGC | 960 |
| | AAGAAAGTCA CAATATTACT TCTTTCCTTC CTTTTTTCCT TCTTTCCTTT CTTCTT | 1020 |
| 55 | TTTCTTTCTT TTTAAAATAT ATTGAAGACA ACCAGATATG TATTTGCTAC TCAAGTGTAC | 1080 |
| | AGATCTCCTC AAGAAACATC AAGGGACTCC TGTGTCACAT ACTGTGTTTT TATTTTAACA | 1140 |
| 60 | TGGGTGAGGG AGGCGACCTG ATCAGGGGAG GTGGGGGGTAC ACATCAATTT GAGTTGTTCA | 1200 |
| | | |

| | GGCTACTGAA | ACA'I I AAAA'I | GIGAATICCC | AAACTTTTCT | TTTTGGCTTT | GTCAGGGAAA | 1260 |
|----------------|------------|----------------|------------|------------|------------|------------|------|
| | AGAAAAATAT | CTTTATAAAG | AAATCTTTGG | AAATTAGGAG | AAGGAATTTC | AGGTGGGTTT | 1320 |
| 5 | AAGTCAGAGC | TAGTTCCCCA | ACAGAAAGAT | CATTTGAAAC | CAGTTTTTAT | CCCTTCTCTT | 1380 |
| | TCCTTCCCTT | TCCCTAAATC | AAATCAATAT | TAATTGTGCC | TTATTTCACT | TAACATAGAC | 1440 |
| 10 | TTGAATTATT | TTTAGGGAAA | GCCCCTATAA | TGAATTCAGA | AATCACTACA | AGCAGCATTA | 1500 |
| 10 | AGACTGAAGT | TGGAATATTC | TGTTGACCAT | AAAACCTTGA | TATCATTCTG | TGTATATAGA | 1560 |
| | ATGTAAAAGG | AATATTACAG | TGTTAACTGC | CATATATGTA | ATATACACAA | ACTCAATTAG | 1620 |
| 15 | CATTGTAATG | GCCAAATGCA | TTCCCCCATG | CTTTTCTGTT | TTCAAAAAAA | TTGAAAAACA | 1680 |
| | AATCAACTCT | TATCCCCAAC | AGCTGCCTAA | TTTTAGGAGT | CTGACCCTCC | ACATCTCACT | 1740 |
| 20 | GGTGTGGGTG | CATGGGGCTG | TGGAGTGGGT | GTCAGTATGG | ATGTGTCTGA | ATGTGTGAGG | 1800 |
| 20 | CCTTGGAAGG | GACTCTTTCT | GCAGATACTG | TAAATACAAG | TACCATTTTA | ATAAAGCATG | 1860 |
| | TACAATAAAC | CAAAATAAGC | TTGAGTTGGA | CTTTATATAC | AGAACTGTAA | GCCAGTGCAT | 1920 |
| 25 | TATGATACAG | TTGTAAGATT | GTGCATTTGA | TTCAAGATAA | GGAAAAATCT | TGGAAATGAA | 1980 |
| | AAGCAGGCAC | KGGTTAACCA | AGTTGTACAC | ATTGTACCAC | ATTCAGCATA | ACTTTAGGAA | 2040 |
| 30 | GAAATTCCAC | TTTGTGAACA | TTCTCCAGAA | ATCCAAGATT | ATTCAGGTAA | GAATTGGTAT | 2100 |
| - | ATTAAATGTA | CATCTTTTA | CTTTCTATTT | TGATGCCAAC | TGATTATACT | AGACAATTAG | 2160 |
| | CACTCCAGGT | GGTTATTGAA | CACAAAACAG | TAAAAGAATA | TTGCACTGAT | AGATACTAAA | 2220 |
| 35 | TTATTATTTT | ATTAGGTTGA | AAAAGCCCTT | ACTAAAAGCC | CCTCATATAT | CAATTACTTT | 2280 |
| | ATTTCATTAT | GACTACTTAG | GTTCCGGGCT | GGGGACAAGT | TCACTTAAAA | AGGCAATGTT | 2340 |
| 40 | ATTTAACAGG | TCACCAGTTA | AGACTTCTGC | TTTGTAGATA | CATGCAGAAG | CCATCAAACA | 2400 |
| , , | AGGGGGRGCT | TTTAACTGCA | ACAATAAGCT | AAAGTATGTA | AAATACTACA | TTCTATTCAG | 2460 |
| | TCTTGGAGTG | TTTTGTAGAA | AGTTATCTTC | AGCCAAATCT | TTGCTGAAGA | CTGGTTGTGG | 2520 |
| 45 | AGTGTTGGTA | AATGCTTTGT | GTTTTTATGT | AAAATATTTT | СТАААСАААА | AATGTTAAAA | 2580 |
| | GTACATGTCC | TCTGTAGTAA | ACTGATATCT | ATATATATGA | ATCATTCAAG | CCTAAAGTCT | 2640 |
| 50 | AGTAATAAAC | TGTACTTGTG | AATAGAGAAA | CCCTAAATAT | TCATGCAGWA | AAAATTATGC | 2700 |
| - - | GGTCTGTTAA | GAAAAATGAG | TAATTTGTGT | TTTGGACTTG | AAATAAACAG | TGTTCTGTAG | 2760 |
| | ATAATTCCTC | AACTTC | | | | | 2776 |

(2) INFORMATION FOR SEQ ID NO: 79:

60 (i) SEQUENCE CHARACTERISTICS:

229

(A) LENGTH: 1525 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

| | (AI) DECOMICE DEDOCATE I TOM DE LE COMME | |
|-----|--|---------------|
| | CCGCTGCTGA TAACTATGGC ATCCCCCGGG CCTGCAGGAA TTCGGCACGG AGC | CTACGGCG 60 |
| 10 | CCGCCTGGCT CCTGCTGNCA CCTGCAGGCT CGTCGCGGGT GGAGCCCACC CAA | AGACATCA 120 |
| | GCATCAGCGA CCAGCTGGGG GGCCAGGACG TGCCCGTGTT CCGGAACCTG TCC | CCTGCTGG 180 |
| 1.5 | TEGTEGETET CEGCECCETE TTCTCACTEC TATTCCACCT EGECACCCEE GAC | GAGGCGCC 240 |
| 15 | GGCCGCATGC GGASGAGCCA GGCGAGCACA CCCCCCTGTT GGCCCCTGCC ACC | GGCCCAGC 300 |
| | CCCTGCTGCT CTGGAAGCAC TGGCTCCGGG AGCSGGCTTT CTACCAGGTG GGC | CATACTGT 360 |
| 20 | ACATGACCAC CAGGCTCATC GTGAACCTGT CCCAGACCTA CATGGCCATG TAG | CCTCACCT 420 |
| | ACTCGCTCCA CCTGCCCAAG AAGTTCATCG CGACCATTCC CCTGGTGATG TAC | CCTCAGCG 480 |
| 25 | GCTTCTTGTC CTCCTTCCTC ATGAAGCCCA TCAACAAGTG CATTGGGAGG AAC | CATGACCT 540 |
| 25 | ACTTCTCAGG CCTCCTGGTG ATCCTGGCCT TTGCCGCCTG GGTGGCGCTG GCC | GGAGGGAC 600 |
| | TGGGTGTGGC CGTGTACGCA GCGGCTGTGC TGCTGGGTGC TGGCTGTGCC ACC | CATCCTCG 660 |
| 30 | TCACCTCGCT GGCCATGACG GCCGACCTCA TCGGTCCCCA CACGAACAGC GG | ACTKTCGT 720 |
| | GTACGGCTCC ATGAGCTTCT TGGATAAGGT GGCCAATGGG CTGGCAGTCA TG | GCCATCCA 780 |
| 35 | GAGCCTGCAC CCTTGCCCCT CAGAGCTCTG CTGCAGGGCC TGCGTGAGCT TT | TACCACTG 840 |
| 33 | GGCGATGGTG GCTGTGACGG GCGGCGTGGG CGTGGCCGCT GCCCTGTGTC TC | TGTAGCCT 900 |
| | CCTGCTGTGG CCGACCCGCC TGCGACGCTG GGACCGTGAT GCCCGGCCCT GA | CTCCTGAC 960 |
| 40 | AGCCTCCTGC ACCTGTGCAA GGGAACTGTG GGGACGCACG AGGATGCCCC CC | ARGGCCTT 1020 |
| | GGGGAAAAGC CCCCACTGCC CCTCACTCTT CTCTGGACCC CCACCCTCCA TC | CTCACCCA 1080 |
| 45 | GCTCCCGGGG GTGGGGTCGG GTGAGGGCAG CAGGGATGCC CGCCAGGGAC TT | GCAAGGAC 1140 |
| 43 | CCCCTGGGTT TTGAGGGTGT CCCATTCTCA ACTCTAATCC ATCCCAGCCC TC | TGGAGGAT 1200 |
| | TTGGGGTGCC CCTCTCGGCA GGGAACAGGA AGTAGGAATC CCAGAAGGGT CT | GGGGGAAC 1260 |
| 50 | CCTAACCCTG AGCTCAGTCC AGTTCACCCC TCACCTCCAG CCTGGGGGTC TC | CAGACACT 1320 |
| | GCCAGGGCCC CCTCAGGACG GCTGGAGCCT GGAGGAGACA GCCACGGGGT GG | TGGGCTGG 1380 |
| 55 | GCCTGGACCC CACCGTGGTG GGCAGCAGGG CTGCCCGGCA GGCTTGGTGG AC | TCTGCTGG 1440 |
| رر | CAGCAAATAA AGAGATGACG GCAAAAAAAA AAAAAAAAAA | 1500 AAAAAAAA |
| | AAAAAAAAA AAACCCACCG TCCGC | 152 5 |

(2) INFORMATION FOR SEQ ID NO: 80:

| 10 | (i) | (A) LEN (B) TYP (C) STR | HARACTERIST: GTH: 1563 b E: nucleic ANDEDNESS: OLOGY: line | ase pairs acid double | | | |
|----|------------|-------------------------------|--|-----------------------------|------------|------------|------|
| | (xi) |) SEQUENCE I | DESCRIPTION | : SEQ ID NO | : 80: | | |
| | AATTCGGCAC | GAGNCAGAAA | CCTGCGGAAA | ATGGTAGCGA | TGGCGGCTGG | GCCGAGTGGG | 60 |
| 15 | TGTCTGGTGC | CGGCGTTTGG | GCTACGGTTG | TTGTTGGCGA | CTGTGCTTCA | AGCGGTGTCT | 120 |
| | GCTTTTGGGG | CAGAGTTTTC | ATCGGAGGCA | TGCAGAGAGT | TAGGCTTTTC | TAGCAACTTG | 180 |
| 20 | CTTTGCAGCT | CTTGTGATCT | TCTCGGACAG | TTCAACCTGC | TTCAGCTGGA | TCCTGATTGC | 240 |
| 20 | AGAGGATGCT | GTCAGGAGGA | AGCACAATTT | GAAACCAAAA | AGCTGTATGC | AGGAGCTATT | 300 |
| | CTTGAAGTTT | GTGGATGAAA | ATTGGGAAGG | TTCCCTCAAG | TCCAAGCTTT | TGTTAGGAGT | 360 |
| 25 | GATAAACCCA | AACTGTTCAG | AGGACTGCAA | ATCAAGTATG | TCCGTGGTTC | AGACCCTGTA | 420 |
| | TTAAAGCTTT | TGGACGACAA | TGGGAACATT | GCTGAAGAAC | TGAGCATTCT | CAAATGGAAC | 480 |
| 30 | ACAGACAGTG | TAGAAGAATT | CCTGAGTGAA | AAGTTGGAAC | GCATATAAAT | CTTGCTTAAA | 540 |
| 50 | TTTTGTCCTA | TCCTTTTGTT | ACCTTATCAA | ATGAAATATT | ACAGCACCTA | GAAAATAATT | 600 |
| | TAGTTTTGCT | TGCTTCCATT | GATCAGTCTT | TTACTTGAGG | CATTAAATAT | CTAATTAAAT | 660 |
| 35 | CGTGAAATGG | CAGTATAGTC | CATGATATCT | AAGGAGTTGG | CAAGCTTAAC | AAAACCCATT | 720 |
| | TTTTATAAAT | GTCCATCCTC | CTGCATTTGT | TGATACCACT | AACAAAATGC | TTTGTAACAG | 780 |
| 40 | ACTTGCGGTT | AATTATGCAA | ATGATAGTTT | GTGATAATTG | GTCCAGTTTT | ACGAACAACA | 840 |
| 10 | GATTTCTAAA | TTAGAGAGGT | TAACAAGACA | GATGATTACT | ATGCCTCATG | TGCTGTGTGC | 900 |
| | TCTTTGAAAG | GAATGACAGC | AGACTACAAA | GCAAATAAGA | TATACTGAGC | CTCAACAGAT | 960 |
| 45 | TGCCTGCTCC | TCAGAGTCTC | TCCTATTTTT | GTATTACCCA | GCTTTCTTTT | TAATACAAAT | 1020 |
| | GTTATTTATA | GTTTACAATG | AATGCACTGC | ATAAAAACTT | TGTAGCTTCA | TTATTGTAAA | 1080 |
| 50 | ACATATTCAA | GATCCTACAG | TAAGAGTGAA | ACATTCACAA | AGATTTGCGT | TAATGAAGAC | 1140 |
| 50 | TACACAGAAA | ACCTITCTAG | GGATTTGTGT | GGATCAGATA | CATACTTGGC | AAATTTTTGA | 1200 |
| | GTTTTACATT | CTTACAGAAA | AGTCCATTTA | AAAGTGATCA | TTTGTAAGAC | СААААТАТАА | 1260 |
| 55 | ATAAAAAGTT | TCAAAAATCT | ATCTGAATTT | GGAATTCTTC | TGGTTTGTTC | TTTCATGTTT | 1320 |
| | AAAAATGATG | TTTTTCAATG | CATTTTTTC | ATGTAAGCCC | TTTTTTTAGC | СААААТСТАА | 1380 |
| 60 | AAATGGCTGT | AATATTTAAA | ACTTATAACA | TCTTATTGTT | GGTAATAGTG | CTTTATATTT | 1440 |
| | | | | | | | |

| | GTCTGATTTT ATTTTTCAAA GTTTTTTCAT TTATGAACAC ATTTTCATTG GTATATTATT | 1500 |
|----|---|------|
| | TAAGGAATAT CTCTTGATAT AGAATTTTTA TATTAAAAAT GATTTTCTT TGCTTAAAAA | 1560 |
| 5 | AAA | 1563 |
| | | |
| 10 | 46 | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 81: | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1020 base pairs | |
| 15 | (B) TYPE: nucleic acid (C) STRANDEDNESS: double | |
| 15 | (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81: | |
| 20 | TGCACGCTGG CCATGTGGGN GTTGGGCCAC TGCGACCCCC GGCGCTGCAC GGGCCGCAAG | 60 |
| | CTGGCCCGCC TGGGGCTGGT GCGCTGCCTG CGCCTGGGCC ACAGATTCGG CGGTCTGGTG | 120 |
| 25 | CTGAGCCCCG TGGGCAAGCA GTACGCGTCC CCCGCAGACA GACAGCTGGT GGCGCAGTCT | 180 |
| 23 | GGGGTCGCCG TCATCGACTG CTCCTGGGCC AGGCTGGACG AGACACCGTT TGGGAAGATG | 240 |
| | CGAGGGAGCC ACTTGCGCCT GTTGCCCTAC CTGGTGGCCG CCAACCCCGT GAACTATGGC | 300 |
| 30 | CGGCCCTACA GACTITCCTG CGTGGAAGCG TTTGCTGCCA CCTTCTGCAT CGTAGGCTTT | 360 |
| | CCAGACCTTG CTGTCATTTT GCTGCGGAAG TITAAATGGG GCAAGGGCTT CTTGGACCTG | 420 |
| 35 | AACCGCCAGC TCCTGGACAA GTACGCGGCC TGCGGCAGCC CGGAGGAGGT GCTGCAGGCG | 480 |
| 33 | GAGCAGGAGT TCTTGGCCAA TGCCAAGGAG AGCCCCCAGG AGGAGGAGAT CGATCCCTTC | 540 |
| | GATGTGGATT CAGGGAGAGA GTTTGGAAAC CCCAACAGGC CTGTGGCCAG CACCCGGCTG | 600 |
| 40 | CCCTCGGACA CTGATGACAG TGATGCGTCT GAGGACCCAG GGCCTKGCGC CGAGCGCGGA | 660 |
| | GGAGCCAGCA GCAGCTGCTG TGAAGAGGAG CAGACGCAGG GACGGGGGGC TGAGGCCAGG | 720 |
| 45 | GCCCCGGCTG AGGTTTGGAA AGGAATCAAG AAACGGCAGA GAGACTGAGG GTTGCAGACA | 780 |
| 43 | CATATATTT TGAGGCTGGG TGACGAGAAA ATCTAGAGAC ATGAGGGACA TAAATGGGCC | 840 |
| | TGGCAGCCTC GGCTCTTTGC GGCTGCTGGC AGGACTGAGC TGTCCGGGTT CTCCCCACAC | 900 |
| 50 | TTCCAGCACA GCTGTGCTCT GTGTCCTGCC TCGGCGCTCT CGCAAATGAA GCTGCAGGCC | 960 |
| | AAGAAAAAA AAAAAAAAA AAAAAAAAAA AAAAAAAA | 1020 |
| 55 | | |
| | (2) INFORMATION FOR SEQ ID NO: 82: | |

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 770 base pairs

232

| | (B) | TYPE: | nucleic | acid | | |
|------|--------|---------|------------|--------|--------|-----|
| | (C) | STRANI | DEDNESS: | double | 9 | |
| | (D) | TOPOLO | OGY: line | ear | | |
| (xi) | SECUEN | ICE DES | CRIPTION | ı. SEO | TD NO. | 82. |
| (~1) | SECOT | ver br | CITTLITION | v. 5EQ | ID NO. | 04. |

TCGACCCACG CGTCCGGCC GCCGTAGCGC GTCTTGGGTC TCCCGGCTGC CGCTGCTGCC 60 GCCGCCGCCT CGGGTCGTGG AGCCAGGAGC GACGTCACCG CCATGGCAGG CATCAAAGCT 120 10 TTGATTAGTT TGTCCTTTGG AGGAGCAATC GGACTGATGT TTTTTRATGCT TGGATGTGCC 180 CTTCCAATAT ACAACAAATA CTGGCCCCTC TTTGTTCTAT TTTTTTACAT CCTTTCACCT 240 15 ATTCCATACT GCATAGCAAG AAGATTAGTG GATGATACAG ATGCTATGAG TAACGCTTGT 300 AAGGAACTTG CCATCTTTCT TACAACGGC ATTGTCGTGT CAGCTTTTGG ACTCCCTATT 360 GTATTTGCCA GAGCACATCT GATTGAGTGG GGAGCTTGTG CACTTGTTCT CACAGGAAAC 420 20 ACAGTCATCT TTGCAACTAT ACTAGGCTTT TTCTTGGTCT TTGGAAGCAA TGACGACTTC 480 AGCTGGCAGC AGTGGTGAAA AGAAATTACT GAACTATTGT CAAATGGACT TCCTGTCATT 540 25 TGTTGGCCAT TCACGCACAC AGGAGATGGG GCAGTTAATG CTGAATGGTA TAGCAAGCCT 600 CTTGGGGGTA TTTTAGGTGC TCCCTTCTCA CTTTTATTGT AAGCATACTA TTTTCACAGA 660 GACTTGCTGA AGGATTAAAA GGATTTTCTC TTTTGGAAAA AAAAAAAAA AAAAACYCGA 720 30 GGGGGGCCC GTWCCCATTC SCCCYATATG AATTCCNTTT TTACAATCCC 770

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(2) INFORMATION FOR SEQ ID NO: 83:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 481 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

45 GAATTCGGCA CGAGCATAGT GTTAACCACT AGAATTCACT GCCCTTCCTA TCCAAAAATG 60 ACACTACTGA TCATTTTTCT TCCTTTTSCT TTTACAACAT TMACAAATTC AGGTGGCTCT 120 50 TTCCCAGTAC GGTAGGCTGA TTCGTATGGA TGCACCACGG TTGGTGACTC CCCCCACCCC 180 ACAGAGTTTC TGGCGTTCAT TCGGTTGAAC CCAAGGCCAG CAAGGGCTGA CTGGGAACAA 240 ACCGAACACT AGGCCGTGAA CCAATCGTCT CTCCGTGCCC GGGAGCGAMC CCGGGGGCCT 300 55 TTCACTCTCC CAAGGACTCC ANGGGGGGGC CGGGTACCCA ATTCCGCCCC TATAGTGAAT 360 CCGTNATTAC AATTCCACNT GGGCCGTCCN TTTTTACAAA CGTTCCGTTG AACTGGGAAA 420 60 AACCCCTTGG CGGTTTACCC CAACTTTAAT CCGCCTTTGC AAGCACATCC CCCCCCTTTT 480

| | С | 481 |
|----|--|-----|
| 5 | | |
| | (2) INFORMATION FOR SEQ ID NO: 84: | |
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 644 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84: | |
| | GCTGGGATAG AGCATGAAAG GAGAACTGCT CCCTTTTCTG TTTCTCACAG TTTGGTTATG | 60 |
| 20 | GCTTTATAAA CTTKTATTTG GTGAAAGCCC CAGATACCCA AATGTCATTG GCAAAACTTA | 120 |
| 20 | TTTTTTTTC TGGACAGATC AGATTTCTAG AGAGAGCAGA TTTCTAGAGA GATTAGCATT | 180 |
| | CATAGTAAGT GAAAATTGTC TAATTTTTT AATCCATGCT ATTACTGGGC AGTAGGTCTA | 240 |
| 25 | ATTTTTTTT ACAAAAAATA GATCTATTTT CCTTATATAT TGATTTAGAA TCTTAAGTTA | 300 |
| | GAATTTATA GAAGAAATGT CTGAGCAGTT CTATGTATGG AGGAGCAATT CAGCTTTTCA | 360 |
| 30 | GCAGCAACTT TATCTTTTGC CACTAGAGGG AGATCTGTGG TTGCTTTCTC CTTTGGAGAA | 420 |
| 30 | TAGCTGCTTT GCTTTTATTT TTAATTTCTA AGGTTGGAAT AGAACTTATT CTCAAAATTC | 480 |
| | CTTTAGTGTT ATTAAATATT TTCATTTATT AGTCAAAGGT AAGTTAATTA AGCTTGTTTA | 540 |
| 35 | ATGATGCCAA TCTTATGCTT TTCTGTAATC TTCAATTTTT AATAAATGTG AGTTAGATAC | 600 |
| | TAAGTGAAAA AAAAAAAAAA AAAAAAAAA AAAAAAAA | 644 |
| 40 | | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 85: | |
| 45 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1351 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| 50 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85: | |
| | GGCACGAGTG CGCASGCGTG GGGCTCTCTC CTTGTCAGTC GGCGCCGCGT GCGGGCTGGT | 60 |
| 55 | GGCTCTGTGG CAGCGGCGGC GGCAGGACTC CGGCACTATG AGCGGCTTCA GCACCGAGGA | 120 |
| دد | GCGCGCCGCG CCNTTCTCCC TGGAGTACCG AGTCTTCCTC AAAAATGAGA AAGGACAATA | 180 |
| | TATATCTCCA TTTCATGATA TTCCAATTTA TGCAGATAAG GATGTGTTTC ACATGGTAGT | 240 |
| 60 | ጥናኔ እርሞእናርን ርርርጥንርምርጥል እጥናርንልእእያጥ ርርልርልጥንርርጥ እርልልልርርልርር ርጥጥያልእርርር | 300 |

| | TATTAAACAA | GATGTGAAAA | AAGGAAAACT | TCGCTATGTT | GCGAATTTGT | TCCCGTATAA | 360 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | AGGATATATC | TGGAACTATG | GTGCCATCCC | TCAGACTTGG | GAAGACCCAG | GGCACAATGA | 420 |
| J | TAAACATACT | GGCTGTTGTG | GTGACAATGA | CCCAATTGAT | GTGTGTGAAA | TTGGAAGCAA | 480 |
| | GGTATGTGCA | AGAGGTGAAA | TAATTGGCGT | GAAAGTTCTA | GGCATATTGG | CTATGATTGA | 540 |
| 10 | CGAAGGGGAA | ACCGACTGGA | AAGTCATTGC | CATTAATGTG | GATGATCCTG | ATGCAGCCAA | 600 |
| | TTATAATGAT | ATCAATGATG | TCAAACGGCT | GAAACCTGGC | TACTTAGAAG | CTACTGTGGA | 660 |
| 15 | CTGGTTTAGA | AGGTATAAGG | TTCCTGATGG | AAAACCAGAA | AATGAGTTTG | CGTTTAATGC | 720 |
| 13 | AGAATTTAAA | GATAAGGACT | TTGCCATTGA | TATTATTAAA | AGCACTCATG | ACCATTGGAA | 780 |
| | AGCATTAGTG | ACTAAGAAAA | CGAATGGAAA | AGGAATCAGT | TGCATGAATA | CAACTTTGTC | 840 |
| 20 | TGAGAGCCCC | TTCAAGTGTG | ATCCTGATGC | TGCCAGAGCC | ATTGTGGATG | CTTTACCACC | 900 |
| | ACCCTGTGAA | TCTGCCTGCA | CAGTACCAAC | AGACGTGGAT | AAGTGGTTCC | ATCACCAGAA | 960 |
| 25 | AAACTAATGA | GATTTCTCTG | GAATACAAGC | TGATATTGCT | ACATCGTGTT | CATCTGGATG | 1020 |
| | TATTAGAAGT | AAAAGTAGTA | GCTTTTCAAA | GCTTTAAATT | TGTAGAACTC | ATCTAACTAA | 1080 |
| | AGTAAATTCT | GCTGTGACTA | ATCCAATATA | CTCAGAATGT | TATCCATCTA | AAGCATTTTT | 1140 |
| 30 | CATATCTCAA | CTAAGATAAC | TTTTAGCACA | TGCTTAAATA | TCAAAGCAGT | TGTCATTTGG | 1200 |
| | AAGTCACTTG | TGAATAGATG | TGCAAGGGGA | GCACATATTG | GATGTATATG | TTACCATATG | 1260 |
| 35 | TTAGGAAATA | AAATTATTTT | GCTGAAAAA | АААААААА | AACCNCGGGG | GGGGCCCCGG | 1320 |
| | TCCCCATTTG | GCCCTTTGGG | GGGNGGTTTT | A | | | 1351 |

45

(2) INFORMATION FOR SEQ ID NO: 86:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2527 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

CTCTTGCTAC CTTCCCGGCG CAGAGAACCC CGGCTGCTCA GCGCGCTCCG GGGTCATGGA 60

GATCCCCGGG AGCCTGTGCA AGAAAGTCAA GCTGAGCAAT AACGCGCAGA ACTGGGGAAT 120

55 GCAGAGAGCA ACCAATGTCA CCTACCAAGC CCATCATGTC AGCAGGAACA AGAGAGGTCA 180

GGTGGTGGGG ACCAGAGGTG GCTTTCGTGG TTGCACAGTT TGGCTAACAG GCTTGTCTCG 240

AGCGGGAAAG ACTACTGTGA GCATGGCCTT GGAGGAGTAC CTGGTTTGTC ATGGTATTCC 300

| | ATGCTACACT | CTGGATGGTG | ACAATATTCG | TCAAGGTCTC | AATAAAAATC | TTGGCTTTAG | 360 |
|----|------------|------------|------------|---------------------|------------|------------|------|
| | TCCTGAAGAC | AGAGAAGAGA | ATGTTCGACG | CATCGCAGAA | GTTGCTAAAC | TGTTTGCAGA | 420 |
| 5 | TGCTGGCTTA | GTGTGCATCA | CAAGTTTCAT | ATCACCTTAC | ACTCAGGATC | GCAACAATGC | 480 |
| | AAGGCAAATT | CATGAAGGTG | CAAGTTTACC | GTTTTTTGAA | GTATTTGTTG | ATGCTCCTCT | 540 |
| 10 | GCATGTTTGT | GAACAGAGGG | ATGTCAAAGG | ACTCTACAAA | AAAGCCCGGG | CAGGAGAAAT | 600 |
| 10 | TAAAGGTTTC | ACTGGGATCG | ATTCTGAATA | TGAAAAGCCA | GAGGCCCCTG | AGTTGGTGCT | 660 |
| | GAAAACAGAC | TCCTGTGATG | TAAATGACTG | TGTCCAGCAA | GTTGTGGAAC | TTCTACAGGA | 720 |
| 15 | ACGGGATATT | GTACCTGTGG | ATGCATCTTA | TGAAGTAAAA | GAACTATATG | TGCCAGAAAA | 780 |
| | TAAACTTCAT | TTGGCAAAAA | CAGATGCGGA | AACATTACCA | GCACTGAAAA | TTAATAAAGT | 840 |
| 20 | GGATATGCAG | TGGGTGCAGG | TTTTGGCAGA | AGGTTGGGCA | ACCCCATTGA | ATGGCTTTAT | 900 |
| 20 | GAGAGAGAGG | GAGTACTTGC | AGTGCCTTCA | TTTTGATTGT | CTTCTGGATG | GAGGTGTCAT | 960 |
| | TAACTTGTCA | GTACCTATAG | TTCTGACTGC | GACTCATGAA | GATAAAGAGA | GGCTGGACGG | 1020 |
| 25 | CTGTACAGCA | TTTGCTCTGA | TGTATGAGGG | CCGCCGTGTG | GCCATTCTTC | GCAATCCAGA | 1080 |
| | GTTTTTTGAG | CACAGGAAAG | AGGAGCGCTG | TGCCAGACAG | TGGGGAACGA | CATGCAAGAA | 1140 |
| 30 | CCACCCCTAT | ATTAAGATGG | TGATGGAACA | AGGAGATTGG | CTGATTGGAG | GAGATCTTCA | 1200 |
| 50 | AGTCTTGGAT | CGAGTTTATT | GGAATGATGG | TCTTGATCAG | TATCGTCTTA | CTCCTACTGA | 1260 |
| | GCTAAAGCAG | AAATTTAAAG | ATATGAATGC | TGATGCTGTC | TTTGCATTTC | AACTACGCAA | 1320 |
| 35 | CCCAGTGCAC | AATGGACATG | CCCTGTTAAT | GCAGGATACC | CATAAGCAAC | TTCTAGAGAG | 1380 |
| | GGGCTACCGG | CGCCCTGTCC | TCCTCCTCCA | CCCTCTGGGT | GGCTGGACAA | AGGATGACGA | 1440 |
| 40 | TGTTCCTTTG | ATGTGGCGTA | TGAAGCAGCA | TGCTGCAGTG | TTGGAGGAAG | GAGTTCTGAA | 1500 |
| 10 | TCCTGAGACG | ACAGTGGTGG | CCATCTTCCC | ATCTCCCATG | ATGTATGCTG | GACCAACTGA | 1560 |
| | GGTCCAGTGG | CATTGCAGAG | CACGGATGGT | TGCAGGAGCC | AACTTTTACA | TTGTTGGACG | 1620 |
| 45 | AGACCCTGCT | GGCATGCCTC | ATCCAGAAAC | AGGGAAGGAT | CTTTATGAGC | CAAGTCATGG | 1680 |
| | TGCCAAAGTG | CTGACGATGG | CCCCTGGTTT | AATCACT TT G | GAAATAGTTC | CCTTTCGAGT | 1740 |
| 50 | TGCAGCTTAC | AACAAGAAAA | AGAAGCGTAT | GGACTACTAT | GACTCTGAAC | ACCATGAAGA | 1800 |
| | CTTTGAATTT | ATTTCAGGAA | CACGAATGCG | CAAACTTGCT | CGAGAAGGCC | AGAAACCACC | 1860 |
| | TGAAGGTTTC | ATGGCTCCCA | AGGCTTGGAC | CGTGCTGACA | GAATACTACA | AATCCTTGGA | 1920 |
| 55 | GAAAGCTTAG | GCTGTTAACC | CAGTCACTCC | ACCTTTGACA | CATTACTAGT | AACAAGAGGG | 1980 |
| | GACCACATAG | TCTCTGTTGG | CATTTCTTTG | TGGTGTCTGT | CTGGACATGC | TTCCTAAAAA | 2040 |
| 60 | CAGACCATTT | TCCTTAACTT | GCATCAGTTT | TGGTCTGCCT | TATGAGTTCT | GTTTTGAACA | 2100 |

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| | AGTGTAACAC | ACTGATGGTT | TTAATGTATC | TTTTCCACTT | ATTATAGTTA | TATTCCTACA | 2160 |
|----|------------|------------|------------|------------|------------|------------|------|
| | ATACAATTT | AAAATTGTCT | TTTTATATTA | TATTTATGCT | TCTGTGTCAT | GATTTTTTCA | 2220 |
| 5 | AGCTGTTATA | TTAGTTGTAA | CCAGTAGTAT | TCACATTAAA | TCTTGCTTTT | TTTCCCCTTA | 2280 |
| | AAAAAAGAAA | AAAATTACCA | AACAATAAAC | TTGGCTAGAC | CTTGTTTTGA | GGATTITACA | 2340 |
| 10 | AGACCTTTGT | AGCGATTAGA | TTTTTTTCT | ACATTGAAAA | TAGAAACTGC | TTCCTTTCTT | 2400 |
| 10 | CTTTCCAGTC | AGCTATTGGT | CTTTCCAGCT | GTTATAATCT | AAAGTATTCT | TATGATCTGT | 2460 |
| | GTAAGCTCTG | AATGAACTTC | TTTACTCAAT | AAAATTAAAT | TTTTGGCTTC | ТТААААААА | 2520 |
| 15 | АААААА | | | | | | 2527 |

20 (2) INFORMATION FOR SEQ ID NO: 87:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2566 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

CCCAAGAATT CGGCACGAGC GNGGCAWAAK TGGGATTTCT GAAACCTGTA GGCCCCAAGC

60

CCATCAACTT GCCCAAAGAA GATTCCAAAC CTACATTTCC CTGGCCTSCT GGAAACAAGC 120 CATCTCTTCA CAGTGTAAAC CAAGACCATG ACTTAAAGCC ACTAGGCCGA AATCTGGGCC 180 35 TACTCCTCCA ACCTCAGAAA ATGAACAGAA GCAAGCKTTT CCCAAATTGA CTGGGGTTAA 240 AGGGAAATTT ATGTCAGCAT CACAAGATCT TGAACCCAAG CCCCTCTTCC CCAAACCCGC 300 40 CTTTGGCCAG AAGCCGCCC TAAGTACCGA GAACTCCCAT GAAGACGAAA GCCCCATGAA 360 GAATGTGTCT TCATCAAAAG GGTCCCCAGC TCCCCTGGGA GTCAGGTCCA AAAGCGGCCC 420 TTTAAAACCA GCAAGGGAAG ACTCAGAAAA TAAAGACCAT GCAGGGGAGA TTTCAAGTTT 480 45 GCCCTTTCCT GGAGTGGTTT TGAAACCTGC TGCGAGCAGG GGAGGCCCAG GTCTCTCCAA 540 AAATGGTGAA GAAAAAAAGG AAGATAGGAA GATAGATGCT GCTAAGAACA CCTTCCAGAG 600 50 CAAAATAAAT CAGGAAGAGT TGGCCTCAGG GACTCCTCCT GCCAGGTTCC CTAAGGCCCC 660 TTCTAAGCTG ACAGTGGGG GGCCATGGGG CCAAAGTCAG GAAAAGGAAA AGGGAGACAA 720 GAATTCAGCC ACCCGAAAC AGAAGCCATT GCCTCCCTTG TTTACCTTGG GTCCACCTCC 780 55 ACCAAAACCC AACAGACCAC CAAATGTTGA CCTGACGAAA TTCCACAAAA CCTCTTCTGG 840 AAACAGTACT AGCAAAGGCC AGACGTCTTA CTCAACAACT TCCCTGCCAC CACCTCCACC 900 60 ATCCCATCCG GCCAGCCAAC CACCATTGCC AGCATCTCAC CCATCACAAC CACCAGTCCC 960

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| | AAGCCTACCT | CCCAGAAACA | TTAAACCTCC | GITTGACCTA | AAAAGCCCTG | TCAATGAAGA | 1020 |
|------------|------------|------------|------------|------------|------------|------------|------|
| 5 | CAATCAAGAT | GGTGTCACGC | ACTCTGATGG | TGCTGGAAAT | CTAGATGAGG | AACAAGACAG | 1080 |
| .5 | TGAAGGAGAA | ACATATGAAG | ACATAGAAGC | ATCCAAAGAA | AGAGAGAAGA | AAAGGGAAAA | 1140 |
| | GGAAGAAAAG | AAGAGGTTAG | AGCTGGAGAA | AAAGGAACAG | AAAGAGAAAG | AAAAGAAAGA | 1200 |
| 10 | ACAAGAAATA | AAGAAGAAAT | TTAAACTAAC | AGGCCCTATT | CAAGTCATCC | ATCTTGCAAA | 1260 |
| | AGCTTGTTGT | GATGTCAAAG | GAGGAAAGAA | TGAACTGAGC | TTCAAGCAAG | GAGAGCAAAT | 1320 |
| 15 | TGAAATCATC | CGCATCACAG | ACAACCCAGA | AGGAAAATGG | TTGGGCAGAA | CAGCAAGGGG | 1380 |
| 13 | TTCATATGGC | TATATTAAAA | CAACTGCTGT | AGAGATTGAC | TATGATTCTT | TGAAACTGAA | 1440 |
| | AAAAGACTCT | CTTGGTGCCC | CTTCAAGACC | TATTGAAGAT | GACCAAGAAG | TATATGATGA | 1500 |
| 20 | TGTTGCAGAG | CAGGATGATA | TTAGCAGCCA | CAGTCAGAGT | GGAAGTGGAG | GGATATTCCC | 1560 |
| | TCCACCACCA | GATGATGACA | TTTATGATGG | GATTGAAGAG | GAAGATGCTG | ATGATGGCTC | 1620 |
| 25 | CACACTACAG | GTTCAAGAGA | AGAGTAATAC | GTGGTCCTGG | GGGATTTTGA | AGATGTTAAA | 1680 |
| 2 5 | GGGAAAAGAT | GACAGAAAGA | AAAGTATACG | AGAGAAACCT | AAAGTCTCTG | ACTCAGACAA | 1740 |
| | TAATGAAGGT | TCATCTTTCC | CTGCTCCTCC | TAAACAATTG | GACATGGGAG | ATGAAGTTTA | 1800 |
| 30 | CGATGATGTG | GATACCTCTG | ATTTCCCTGT | TTCATCAGCA | GAGATGAGTC | AAGGAACTAA | 1860 |
| | TGTTGGAAAA | GCTAAGACAG | AAGAAAAGGA | CCTTAAGAAG | CTAAAAAAGC | AGRAAAAARA | 1920 |
| 35 | ARAAAAAGAC | TTCAGGAAAA | ATTTAAATA | TGATGGTGAA | ATTAGAGTCC | TATATTCAAC | 1980 |
| | TAAAGTTACA | ACTTCCATAA | CTTCTAAAAA | GTGGGGAACC | AGAGATCTAC | AGGTAAAACC | 2040 |
| | TGGTGAATCT | CTAGAAGTTA | TACAAACCAC | AGATGACACA | AAAGTTCTCT | GCAGAAATGA | 2100 |
| 40 | AGAAGGGAAA | TATGGTTATG | TCCTTCGGAG | TTACCTAGCG | GACAATGATG | GAGAGATCTA | 2160 |
| | TGATGATATT | GCTGATGGCT | GCATCTATGA | CAATGACTAG | CACTCAACTT | TGGTCATTCT | 2220 |
| 45 | GCTGTGTTCA | TTAGGTGCCA | ATGTGAAGTC | TGGATTTTAA | TTGGCATGTT | ATTGGGTATC | 2280 |
| | AAGAAAATTA | ATGCACAAAA | CCACTTATTA | TCATTTGTTA | TGAAATCCCA | ATTATCTTTA | 2340 |
| | CAAAGTGTTT | AAAGTTTGAA | CATAGAAAAT | AATCTCTCTG | CTTAATTGTT | ATCTCAGAAG | 2400 |
| 50 | ACTACATTAG | TGAGATGTAA | GAATTATTAA | ATATTCCATT | TCCGCTTTGG | CTACAATTAT | 2460 |
| | GAAGAAGTTG | AAGGTACTTC | TTTTAGACCA | CCAGTAAATA | ATCCTCCTTC | AAAAAAAA | 2520 |
| 55 | ААГААААААА | AAAAAAAAA | ACTCGAGGGG | GGGCCCGGTA | CCCAAT | | 2566 |
| | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 88:

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| 5 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 540 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
|----------|---|-----|
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88: | |
| 10 | GAATTCGGCA CGAGGCTTTC TGTGTCCTCT GTGGCTGCTT TAGTGTGCCA CCAGGGGCAG | 60 |
| 10 | ACTTGGGTGG GTTGCAGCAG AGATGGCATG GCCCTCAAGG TCCAAGATGT TTACTCTCTT | 120 |
| | GCCGGTCCTC TGTTATCTCT GGTCTTTGTG GTTGCCACAG TTTTCTTGGA TCCAGGAGTT | 180 |
| 15 | AAAGGCAGTC CTGAGGGATG ATGGCCTCAT CTCCGCAGTT GCYTGGAATG CTGAATTTCA | 240 |
| | GACGTGCTAA AGGAGGGTTG CAGACATTGT GTGGWATGCA TTCAGACCCC AGATGTGGGT | 300 |
| 20 | GCAGGAAGGC AGGCATGGCA CAGCCAGGTA GAGACTGGTT TCCAGGCCCA AGCAGCCTTC | 360 |
| 20 | AGCAGCTGTG CGCCTTGTTT CTGATGTTGT TTGGGAGTAA GAATAATGTA GACATGGGGG | 420 |
| | GTCATGARGC TCAATAAAAA CTTCAAGGAA ACCTCCCATG GCATGGTTGG GCGCAGTGAC | 480 |
| 25 | TCATGCCTGT AACCCCAGCA CTGTGGAATG CCAAGGTGGA AGGATCGCTT GAGGCCAAGA | 540 |
| 30 35 | (2) INFORMATION FOR SEQ ID NO: 89: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1863 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89: | |
| 40 | TCGACCCACG CGTCCGGCGA GATCCCTACC GCAGTAGCCG CCTCTGCCGC CGCGGAGCTT | 60 |
| | CCCGAACCTC TTCAGCCGCC CGGAGCCGCT CCCGGAGCCC GGCCGTAGAG GCTGCAATCG | 120 |
| 45 | CAGCCGGGAG CCCGCAGCCC GCGCCCCGAG CCCGCCGCCG CCCTTCGAGG GCGCCCCAGG | 180 |
| | CCGCGCCATG GTGAAGGTGA CGTTCAACTC CGCTCTGGCC CAGAAGGAGG CCAAGAAGGA | 240 |
| | CGAGCCCAAG AGCGCCGAGG AGGCGCTCAT CATCCCCCC GACGCCGTCG CGGTGGACTG | 300 |
| 50 | CAAGGACCCA GATGATGTGG TACCAGTTGG CCAAAGAAGA GCCTGGTGTT GGTGCATGTG | 360 |
| | CTTTGGACTA GCATTTATGC TTGCAGGTGT TATTCTAGGA GGAGCATACT TGTACAAATA | 420 |
| | TTTTGCACTT CAACCAGATG ACGTGTACTA CTGTGGAATA AAGTACATCA AAGATGATGT | 480 |

CATCTTAAAT GAGCCCTCTG CAGATGCCCC AGCTGCTCTC TACCAGACAA TTGAAGAAAA

TATTAAAATC TTTGAAGAAG AAGAAGTTGA ATTTATCAGT GTGCCTGTCC CAGAGTTTGC

AGATAGTGAT CCTGCCAACA TTGTTCATGA CTTTAACAAG AAACTTACAG CCTATTTAGA

540

660

55

| | TCTTAACCTG | GATAAGTGCT | ATGTGATCCC | TCTGAACACT | TCCATTGTTA | TGCCACCCAG | 720 |
|-----|------------|-----------------------|-----------------------------|------------|------------|------------|------|
| _ | AAACCTACTG | GAGTTACTTA | TTAACATCAA | GGCTGGAACC | TATTTGCCTC | AGTCCTATCT | 780 |
| 5 | GATTCATGAG | CACATGGTTA | TTACTGATCG | CATTGAAAAC | ATTGATCACC | TGGGTTTCTT | 840 |
| | TATTTATCGA | CTGTGTCATG | ACAAGGAAAC | TTACAAACTG | CAACGCAGAG | AAACTATTAA | 900 |
| 10 | AGGTATTCAG | AAACGTGAAG | CCAGCAATTG | TTTCGCAATT | CGGCATTTTG | AAAACAAATT | 960 |
| | TGCCGTGGAA | ACTITAATTT | GTTCTTGAAC | AGTCAAGAAA | AACATTATTG | AGGAAAATTA | 1020 |
| | ATATCACAGC | ATAACCCCAC | CCTTTACATT | TTGTGCAGTG | ATTATTTTTT | AAAGTCTTCT | 1080 |
| 15 | TTCATGTAAG | TAGCAAACAG | GGCTTTACTA | TCTTTTCATC | TCATTAATTC | AATTAAAACC | 1140 |
| | ATTACCTTAA | AATTTTTTTC | TTTCGAAGTG | TGGTGTCTTT | TATATTTGAA | TTAGTAACTG | 1200 |
| 20 | TATGAAGTCA | TAGATAATAG | TACATGTCAC | CTTAGGTAGT | AGGAAGAATT | ACAATTTCTT | 1260 |
| | TAAATCATTT | ATCTGGATTT | TTATGTTTTA | TTAGCATTTT | CAAGAAGACG | GATTATCTAG | 1320 |
| 0.5 | AGAATAATCA | TATATATGCA | TACGTAAAAA | TGGACCACAG | TGACTTATTT | GTAGTTGTTA | 1380 |
| 25 | GTTGCCCTGC | TACCTAGTTT | GTTAGTGCAT | TTGAGCACAC | ATTTTAATTT | TCCTCTAATT | 1440 |
| | AAAATGTGCA | GTATTTTCAG | TGTCAAATAT | ATTTAACTAT | TTAGAGAATG | ATTTCCACCT | 1500 |
| 30 | TTATGTTTTA | ATATCCTAGG | CATCTGCTGT | AATAATATTT | TAGAAAATGT | TTGGAATTTA | 1560 |
| | AGAAATAACT | TGTGTTACTA | ATTTGTATAA | CCCATATCTG | TGCAATGGAA | TATAAATATC | 1620 |
| 25 | ACAAAGTTGT | TTAACTAGAC | TGCGTGTTGT | TTTTCCCGTA | ТААТААААСС | AAAGAATAGT | 1680 |
| 35 | TTGGTTCTTC | AAATCTTAAG | AGAATCCACA | TAAAAGAAGA | AACTATTTT | TAAAAATTCA | 1740 |
| | СТТСТАТАТА | TACAATGAGT | AAAATCACAG | ATTTTTCTT | ТАААТАААТ | TAAGTCATTT | 1800 |
| 40 | ТААТААСТАА | ACCAGATTCT | TTGTGATACT | ATTAANGTAA | CATTTAGCCC | САААААААА | 1860 |
| | AAA | | | | | | 1863 |
| 45 | | | | | | | |
| 43 | (0) TMT0DM | AMION FOR C | EO ID NO. 0 | 0. | | | |
| | , | ATION FOR S | - | | | | |
| 50 | (i) | SEQUENCE C (A) LEN | HARACTERIST IGTH: 2478 1 | | | | |

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

> GGCACAGCGG CACGAGGTGA GCTGAGCCGG TGGGTGAGCG GCGGCCACGG CATCCTGTGC 60 TGTGGGGGCT ACGAGGAAAG ATCTAATTAT CATGGACCTG CGACAGTTTC TTATGTGCCT 120

| | GTCCCTGTGC | ACAGCCTTTG | CCTTGAGCAA | ACCCACAGAA | AAGAAGGACC | GTGTACATCA | 180 |
|-----|------------|------------|------------|-------------|------------|------------|------|
| | TGAGCCTCAG | CTCAGTGACA | AGGTTCACAA | TGATGCTCAG | AGTTTTGATT | ATGACCATGA | 240 |
| 5. | TGCCTTCTTG | GGTGCTGAAG | AAGCAAAGAC | CTTTGATCAG | CTGACACCAG | AAGAGAGCAA | 300 |
| | GGAAAGGCTT | GGAAAGATTG | TAAGTAAAAT | AGATGGCGAC | AAGGACGGGT | TTGTCACTGT | 360 |
| 10 | GGATGAGCTC | AAAGACTGGA | TTAAATTTGC | ACAAAAGCGC | TGGATTTACG | AGGATGTAGA | 420 |
| 10 | GCGACAGTGG | AAGGGGCATG | ACCTCAATGA | GGACGGCCTC | GTTTCCTGGG | AGGAGTATAA | 480 |
| | AAATGCCACC | TACGGCTACG | TTTTAGATGA | TCCAGATCCT | GATGATGGAT | TTAACTATAA | 540 |
| 15 | ACAGATGATG | GTTAGAGATG | AGCGGAGGTT | TAAAATGGCA | GACAAGGATG | GAGACCTCAT | 600 |
| | TGCCACCAAG | GAGGAGTTCA | CAGCTTTCCT | GCACCCTGAG | GAGTATGACT | ACATGAAAGA | 660 |
| 20 | TATAGTAGTA | CAGGAAACAA | TGGAAGATAT | AGATAAGAAT | GCTGATGGTT | TCATTGATCT | 720 |
| 20 | AGAAGAGTAT | ATTGGTGACA | TGTACAGCCA | TGATGGGAAT | ACTGATGAGC | CAGAATGGGT | 780 |
| | AAAGACAGAG | CGAGAGCAGT | TTGTTGAGTT | TCGGGATAAG | AACCGTGATG | GGAAGATGGA | 840 |
| 25 | CAAGGAAGAG | ACCAAAGACT | GGATCCTTCC | CTCAGACTAT | GATCATGCAG | AGGCAGAAGC | 900 |
| | CAGGCACCTG | GTCTATGAAT | CAGACCAAAA | CAAGGATGGC | AAGCTTACCA | AGGAGGAGAT | 960 |
| 30 | CGTTGACAAG | TATGACTTAT | TTGTTGGCAG | CCAGGCCACA | GATTTTGGGG | AGGCCTTAGT | 1020 |
| 50 | ACGGCATGAT | GAGTTCTGAG | CTRCGGAGGA | ACCCTCATTT | CCTCAAAAGT | AATTTATTTT | 1080 |
| | TACAGCTTCT | GGTTTCACAT | GAAATTGTTT | GCGCTACTGA | GACTGTTACT | ACAAACTTTT | 1140 |
| 35 | TAAGACATGA | AAAGGCGTAA | TGAAAACCAT | CCCGTCCCCA | TTCCTCCTCC | TCTCTGAGGG | 1200 |
| | ACTGGAGGGA | AGCCGTGCTT | CTGAGGAACA | ACTCTAATTA | GTACACTTGT | GTTTGTAGAT | 1260 |
| 40 | TTACACTTTG | TATTATGTAT | TAACATGGCG | TGTTTATTTT | TGTATTTTTC | TCTGGTTGGG | 1320 |
| | AGTATGATAT | GAAGGATCAA | GATCCTCAAC | TCACACATGT | AGACAAACAT | TAGCTCTTTA | 1380 |
| | CTCTTTCTCA | ACCCCTTTTA | TGATTTTAAT | AATTCTCACT | TAACTAATTT | TGTAAGCCTG | 1440 |
| 45 | AGATCAATAA | GAAATGTTCA | GGAGAGAGGA | AAGAAAAAA | ATATATGCTC | CACAATTTAT | 1500 |
| | ATTTAGAGAG | AGAACACTTA | GTCTTGCCTG | TCAAAAAGTC | CAACATTTCA | TAGGTAGTAG | 1560 |
| 50 | GGGCCACATA | TTACATTCAG | TTGCTATAGG | TCCAGCAACT | GAACCTGCCA | TTACCTGGGC | 1620 |
| 50 | AAGGAAAGAT | CCCTTTGCTC | TAGGAAAGCT | 'TGGCCCAAAT | TGATTTTCTT | CTTTTTCCCC | 1680 |
| | CTGTAGGACT | GACTGTTGGC | TAATTTIGTC | AAGCACAGCT | GTGGTGGGAA | GAGTTAGGGC | 1740 |
| 55 | CAGTGTCTTG | AAAATCAATC | AAGTAGTGAA | TGTGATCTCT | TTGCAGAGCT | ATAGATAGAA | 1800 |
| | ACAGCTGGAA | AACTAAAGGA | AAAATACAAG | TGTTTTCGGG | GCATACATTI | TTTTTCTGGG | 1860 |
| 60 | TGTGCATCTC | TTGAAATGCT | CAAGACTTAA | TTATTTGCCT | TTTGAAATCA | CTGTAAATGC | 1920 |
| ~ ~ | | | | | | | |

| GTCA 2040 |
|-----------|
| PTAT 2100 |
| TTTG 2160 |
| GTGG 2220 |
| ATGC 2280 |
| CAAA 2340 |
| TGCC 2400 |
| CAGC 2460 |
| 2478 |
| |

(2) INFORMATION FOR SEQ ID NO: 91:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2058 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
- 30 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

TCGGCCTTGC TTTTGTGGYC TTCCTCTGTG GCCAGAGCGT TTTCATCACC AAGCCTCCTG 60 35 ATGGCAGTNC CTTCACCGAT ATGTTCAAGA TACTGACGTA TTCCTGCTGT TCCCAGAAGC 120 GAAGTGGAGA GCGCCAGAGT AATGGTGAAG GCATTGGAGT NTTTCAGCAA TCTTCTAAAC 180 40 AAAGTCTGTT TGATTCATGT AAGATGTCTC ATGGTGGGCC ATTTACAGAA GAGAAAGTGG 240 AAGATGTGAA AGCTCTGGTC AAGATTGTCC CTGTTTTCTT GGCTTTGATA CCTTACTGGA 300 CAGTGTATTT CCAAATGCAG ACAACATATG TTTTACAGAG TCTTCATTTG AGGATTCCAG 360 45 AAATTTCAAA TATTACAACC ACTCCTCACA CGCTCCCTGC AGCCTGGCTG ACCATGTTTG 420 ATGCTGTGCT CATCCTCCTG CTCATCCCTC TGAAGGACAA ACTGGTCGAT CCCATTTTGA 480 50 GAAGACATGG CCTGCTCCCA TCCTCCCTGA AGAGGATCGC CGTGGGCATG TTCTTTGTCA 540 600 TGTGCTCRGC CTTTGCTGCA GGAATTTTGG AGAGTAAAAG GCTGAACCTT GTTAAAGAGA AAACCATTAA TCAGACCATC GGCAACGTCG TCTACCATGC TGCCGATCTG TCGCTGTGGT 660 55 GGCAGGTGCC GCAGTACTTG CTGATTGGGA TCAGCGAGAT CTTTGCAAGT ATCGCAGGCC 720 TGGAATTTGC ATACTCAGCT GCCCCCAAGT CCATGCAGAG TGCCATAATG GGCTTGTTCT 780 60 840 TTTTCTTCTC TGGCGTCGGG TCGTTCGTGG GTTCTGGACT GCTGGCACTG GTGTCTATCA

| | AAGCCATCGG | ATGGATGAGC | AGTCACACAG | ACTTTGGTAA | TATTAACGGC | TGCTATTTGA | 900 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | ACTATTACTT | TTTCCTTCTG | GCTGCTATTC | AAGGAGCTAC | CCTCCTGCTT | TTCCTCATTA | 960 |
| 3 | TTTCTGTGAA | ATATGACCAT | CATCGAGACC | ATCAGCGATC | AAGAGCCAAT | GGCGTGCCCA | 1020 |
| | CCAGCAGGAG | GGCCTGACCT | TCCTGAGGCC | ATGTGCGGTT | TCTGAGGCTG | ACATGTCAGT | 1080 |
| 10 | AACTGACTGG | GGTGCACTGA | GAACAGGCAA | GACTTTAAAT | TCCCATAAAA | TGTCTGACTT | 1140 |
| | CACTGAAACT | TGCATGTTGC | CTGGATTGAT | TTCTTCTTTC | CCTCTATCCA | AAGGAGCTTG | 1200 |
| 15 | GTAAGTGCCT | TACTGCAGCG | TGTCTCCTGG | CACGCTGGGC | CCTCCGGGAG | GAGAGCTGCA | 1260 |
| 13 | GATTTCGAGT | ATGTCGCTTG | TCATTCAAGG | TCTCTGTGAA | TCCTCTAGCT | GGGTTCCCTT | 1320 |
| | TTTTACAGAA | ACTCACAAAT | GGAGATTGCA | AAGTCTTGGG | GAACTCCACG | TGTTAGTTGG | 1380 |
| 20 | CATCCCAGTT | TCTTAAACAA | ATAGTATCAC | CTGCTTCCCA | TAGCCATATC | TCACTGTAAA | 1440 |
| | AAAAAAAATT | AATAAACTGT | TACTTATATT | TAAGAAAGTG | AGGATTTTTT | TTTTTAAAG | 1500 |
| 25 | ATAAAAGCAT | GGTCAGATGC | TGCAAGGATT | TTACATAAAT | GCCATATTTA | TGGTTTCCTT | 1560 |
| 23 | CCTGAGAACA | ATCTTGCTCT | TGCCATGTTC | TTTGATTTAG | GCTGGTAGTA | AACACATTTC | 1620 |
| | ATCTGCTGCT | TCAAAAAGTA | CTTACTTTTT | AAACCATCAA | CATTACTTTT | CTTTCTTAAG | 1680 |
| 30 | GCAAGGCATG | CATAAGAGTC | ATTTGAGACC | ATGTGTCCCA | TCTCAAGCCA | CAGAGCAACT | 1740 |
| | CACGGGGTAC | TTCACACCTT | ACCTAGTCAG | AGTGCTTATA | TATAGCTTTA | TTTTGGTACG | 1800 |
| 35 | ATTGAGACTA | AAGACTGATC | ATGGTTGTAT | GTAAGGAAAA | CATTCTTTTG | AACAGAAATA | 1860 |
| 55 | GTGTAATTAA | AAATAATTGA | AAGTGTTAAA | TGTGAACTTG | AGCTGTTTGA | CCAGTCACAT | 1920 |
| | TTTTGTATTG | TTACTGTACG | TGTATCTGGG | GCTTCTCCGT | TTGTTAATAC | TTTTTCTGTA | 1980 |
| 40 | TTTGTTGCTG | TATTTTTGGC | ATAACTTTAT | TATAAAAAGC | ATCTCAAATG | CGAAAWAAAA | 2040 |
| | АААААААА | AAAAAAAC | | | | | 2058 |

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(2) INFORMATION FOR SEQ ID NO: 92:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1411 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

GGCACAGGAG CGACCCGGGA GAAGGAGGGC CAMGAKGCGG AAGCGGAGGA GTCTCCAGGA 60
GACCCGGGGA CAGCATCGCC CAGGCCCCTG TTTGCAGGCC TTTCAGATAT ATCCATCTCA 120

| | CAAGACATCC | CCGTAGAAGG | AGAAATCACC | ATTCCTATGA | GATCTCGCAT | CCGGGAGTTT | 180 |
|----|------------|--------------|-----------------------------|--------------|--------------|--------------|------|
| | GACAGCTCCA | CATTAAATGA | ATCTGTTCGC | AATACCATCA | TGCGTGATCT | AAAAGCTGTT | 240 |
| 5 | GGGAAAAAT | TCATGCATGT | TTTGTACCCA | AGGAAAAGTA | ATACTCTTTT | GAGAGATTGG | 300 |
| | GATTTGTGGG | GCCCTTTGAT | CCTTTGTGTG | ACACTCGCAT | TAATGCTGCA | AAGAGACTCT | 360 |
| 10 | GCAGATAGTG | AAAAAGATGG | AGGCCCCAA | TTTGCAGAGG | TGTTTGTCAT | TGTCTGGTTT | 420 |
| 10 | GGTGCAGTTA | CCATCACCCT | CAACTCAAAA | CTTCTTGGAG | GGAACATATC | TTTTTTCAG | 480 |
| | AGCCTCTGTG | TGCTGGGTTA | CTGTATACTT | CCCTTGACAG | TAGCAATGCT | GATTTGCCGG | 540 |
| 15 | CTGGTACTTT | TGGCTGATCC | AGGACCTGTA | AACTTCATGG | TTCGGCTTTT | TGTGGTGATT | 600 |
| | GTGATGTTTG | CCTGGTCTAT | AGTTGCCTCC | ACAGCTTTCC | TTGCTGATAG | CCAGCCTCCA | 660 |
| 20 | AACCGCAGAG | CCCTAGCTGT | TTATCCTGTT | TTCCTGTTTT | ACTTTGTCAT | CAGTTGGATG | 720 |
| 20 | ATTCTCACCT | TTACTCCTCA | GTAAATCAGG | AATGGGAAAT | TAAAAACCAG | TGAATTGAAA | 780 |
| | GCACATCTGA | AAGATGCAAT | TCACCATGGA | GCTTTGTCTC | TGGCCCTTAT | TTGTCTAATT | 840 |
| 25 | TTGGAGGTAT | TTGATAACTG | AGTAGGTGAG | GAGATTAAAA | GGGAGCCATA | TAGCACTGTC | 900 |
| | ACCCCTTATT | TGAGGAACTG | ATGTTTGAAA | GGCTGTTCTT | TTCTCTCTTA | ATGTCATTTC | 960 |
| 20 | TTTAAAAATA | CATGTGCATA | CTACACACAG | TATATAATGC | CTCCTTAAGG | CATGATGGAG | 1020 |
| 30 | TCACCGTGGT | CCATTIGGGT | GACAACCAGT | GACTTGGGAA | GCACATAGAT | ACATCTTACA | 1080 |
| | AGTTGAATAG | AGTTGATAAC | TATTTTCAGT | TTTGAGAATA | CCAGTTCAGG | TGCAGCTCTT | 1140 |
| 35 | AAACACATTG | CCTTATGACT | ATTAGAATAT | GCCTCTCTT | ТСАТАААТАА | AAATACATGG | 1200 |
| | TCTATATCCA | TTTTCTTTTA | TTTCTCTCTC | TTAAGCTTAA | AAAGGCAATG | AGAGAGGTTA | 1260 |
| 40 | GGAGTGGGTT | ' CATACACGGA | GAATGAGAAA | ACATGCATTA | ACCAATATTC | AGATTTTGAT | 1320 |
| 40 | CAGGGGAAAT | TCTAYACTTG | TTGCAAAAAA | AAAAAAAAA | AAACTCGAGG | GGGGCCCGGT | 1380 |
| | ACCCAATCGC | : NGTATATGAT | CGNAAACAAT | C | | | 1411 |
| 45 | | | | | | | |
| | (2) TNEOPM | MATION FOR S | FO ID NO: 9 | 3. | | | |
| 50 | | SEQUENCE C | _ | | • | | |
| 30 | (1) | (A) LEN | NGTH: 2187 l PE: nucleic | oase pairs | | | |
| | | (C) ST | RANDEDNESS: POLOGY: line | double | | | |
| 55 | / | i) SEQUENCE | | |). q3. | | |
| | • | - | | | | TTTCCAGAAG | 60 |
| | GCTTIGGCTI | 1111110000 | ACIBOOCIC | - CCICCGGAAG | , CGIIICCAAC | . IIICCHUMMU | 00 |

TTTCTCGGGA CGGCAGGAG GGGGTGGGGA CTGCCATATA TAGATCCCGG GAGCAGGGGA 120

| | GCGGGCTAAG | AGTAGAATCG | TGTCGCGCTC | GAGAGCGAGA | GTCACGTCCC | GGCGCTAGCC | 180 |
|------------|------------|------------|------------|------------|------------|------------|------|
| 5 | CAGCCCGACC | CAGGCCCACC | GTGGTGCACG | CAAACCACTT | CCTGGCCATG | CGCTCCCTCC | 240 |
| , | TGCTTCTCAG | CGCCTTCTGC | CTCCTGGAGG | CGGCCCTGGC | CGCCGAGGTG | AAGAAACCTG | 300 |
| | CAGCCGCAGC | AGCTCCTGGC | ACTGCGGAGA | AGTTGAGCCC | CAAGGCGGCC | ACGCTTGCCG | 360 |
| 10 | AGCGCAGCCG | GCCTGGCCTT | CAGCTTGTAC | CAGGCCATGG | CCAAGGACCA | GGCAGTGGAG | 420 |
| | AACATCCTGG | TGTCACCCGT | GCTGGTGGCC | TCGTCGCTGG | GGCTCGTGTC | GCTGGGCGGC | 480 |
| 15 | AAGGCGACCA | CGGCGTCGCA | GGCCAAGGCA | GTGCTGAGCG | CCGAGCAGCT | GCGCGACGAG | 540 |
| 13 | GAGGTGCACG | CCGGCCTGGG | CGAGCTGCTG | CGCTCACTCA | GCAACTCCAC | GGCGCGCAAC | 600 |
| | GTGACCTGGA | AGCTGGGCAG | CCGACTGTAC | GGACCCAGCT | CAGTGAGCTT | CGCTGATGAC | 660 |
| 20 | TTCGTGCGCA | GCAGCAAGCA | GCACTACAAC | TGCGAGCACT | CCAAGATCAA | CTTCCGCGAC | 720 |
| | AAGCGCAGCG | CGCTGCAGTC | CATCAACGAG | TGGGCCGCGC | AGACCACCGA | CGGCAAGCTG | 780 |
| 25 | CCCGAGGTCA | CCAAGGACGT | GGAGCGCACG | GACGGCGCCC | TGTTAGTCAA | CGCCATGTTC | 840 |
| 23 | TTCAAGCCAC | ACTGGGATGA | GAAATTCCAC | CACAAGATGG | TGGACAACCG | TGGCTTCATG | 900 |
| | GTGACTCGGT | CCTATACCGT | GGGTGTCATG | ATGATGCACC | GGACAGGCCT | CTACAACTAC | 960 |
| 30 | TACGACGACG | AGAAGGAAAA | GCTGCAAATC | GTGGAGATGC | CCCTGGCCCA | CAAGCTCTCC | 1020 |
| | AGCCTCATCA | TCCTCATGCC | CCATCACGTG | GAGCCTCTCG | AGCGCCTTGA | AAAGCTGCTA | 1080 |
| 35 | ACCAAAGAGC | AGCTGAAGAT | CTGGATGGGG | AAGATGCAGA | AGAAGGCTGT | TGCCATCTCC | 1140 |
|),) | TTGCCCAAGG | GTGTGGTGGA | GGTGACCCAT | GACCTGCAGA | AACACCTGGC | TGGGCTGGGC | 1200 |
| | CTGACTGAGG | CCATTGACAA | GAACAAGGCC | GACTTGTCAC | GCATGTCAGG | CAAGAAGGAC | 1260 |
| 40 | CTGTACCTGG | CCAGCGTGTT | CCACGCCACC | GCCTTTGAGT | TGGACACAGA | TGGCAACCCT | 1320 |
| | TTGACCAGAA | TTACGGGCGG | AGGAGTGCGC | ACCCAAGTGT | TCTACGCCGA | CCACCCCTTC | 1380 |
| 15 | ATTTCCTAGT | GCGGGACACC | CAAAGCGGTC | CCTGCTATTC | ATTGGGCGCC | TGGTCCGGCC | 1440 |
| + J | TAAGGGTGAC | AAGATGCGAG | ACGAGTTATA | GGCCTCAGGG | TGCACACAGG | ATGGCAGGAG | 1500 |
| | GCATCCAAAG | GCTCCTGAGA | CACATGGGTG | CTATTGGGGT | TGGGGGGAG | GTGAGGTACC | 1560 |
| 50 | AGCCTTGGAT | ACTCCATGGG | GTGGGGTGGA | AAAGCAGACC | GGGGTTCCCG | TGTGCCTGAG | 1620 |
| | CGGACTTCCC | AGCTAGAATT | CACTCCACTT | GGACATGGGC | CCCAGATACC | ATGATGCTGA | 1680 |
| 55 | GCCCGGAAAC | TCCACATCCT | GTGGGACCTG | GGCCATAGTC | ATTCTGCCTG | CCCTGAAAGT | 1740 |
| ی ر | CCCAGATCAA | GCCTGCCTCA | ATCAGTATTC | ATATTTATAG | CCAGGTACCT | TCTCACCTGT | 1800 |
| | GAGACCAAAT | TGAGCTAGGG | GGGTCAGCCA | GCCCTCTTCT | GACACTAAAA | CACCTCAGCT | 1860 |
| 50 | GCCTCCCCAG | CTCTATCCCA | ACCTCTCCCA | ACTATAAAAC | TAGGTGCTGC | AGCCCCTGGG | 1920 |

| | ACCAGGCACC CCCAGAATGA CCTGGCCGCA GTGAGGCGGA TTGAGAAGGA GCTCCCAGGA | 1980 |
|-----|---|------|
| _ | GGGGCTTCTG GGCAGACTCT GGTCAAGAAG CATCGTGTCT GGCGTTGTGG GGATGAACTT | 2040 |
| 5 | TTTGTTTGT TTCTTCCTTT TTTAGTTCTT CAAAGATAGG GAGGGAAGGG GGAACATGAG | 2100 |
| | CCTTTGTTGC TATCAATCCA AGAACTTATT TGTACATTTT TTTTTTCAAT AAAACTTTTC | 2160 |
| 10 | CAATGACAAA AAAAAAAAA AAAAAAA | 2187 |
| | | |
| 1.5 | | |
| 15 | (2) INFORMATION FOR SEQ ID NO: 94: | |
| 20 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 757 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94: | |
| 25 | GACAGTACGG TCGGATTCCC GGGTCGACCC ACGCGTCCGC GGACGGTGAA GAAGGTGAAG | 60 |
| | ATGGCGGTGG CCAGGGCCGG GGTCTTGGGA GTCCAGTGGC TGCAAAGGGC ATCCCGGAAC | 120 |
| 30 | GTGATGCCGC TGGGCGCACG GACAGCCTCC CACATGACCA AGGACATGTT CCCGGGGCCC | 180 |
| 30 | TATCCTAGGA CCCCAGAAGA ACGGGCCGCC GCCGCCAAGA AGTATAATAT GCGTGTGGAA | 240 |
| | GACTACGAAC CTTACCCGGA TGATGGCATG GGGTATGGCG ACTACCCGAA GCTCCCTGAC | 300 |
| 35 | CGCTCACAGC ATGAGAGAGA TCCATGGTAT AGCTGGGACC AGCCGGGCCT GAGGTTGAAC | 360 |
| | TGGGGTGAAC CGATGCACTG GCACCTAGAC ATGTACAACA GGAACCGTGT GGATACATCC | 420 |
| 40 | CCCACACCTG TTTCTTGGCA TGTCATGTGT ATGCAGCTCT TCGGTTTCCT GGCTTTCATG | 480 |
| 40 | ATATTCATGT GCTGGGTGGG GGACGTGTAC CCTGTCTACC AGCCTGTGGG ACCAAAGCAG | 540 |
| | TATCCTTACA ATAATCTGTA CCTGGAACGA GGCGGTGATC CCTCCAAAGA ACCAGAGCGG | 600 |
| 45 | GTGGTTCACT ATGAGATCTG AGGAGGCTTC GTGGGCTTTT GGGTCCTCTA ACTAGGACTC | 660 |
| | CCTCATTCCT AGAAATTTAA CCTTAATGAA ATCCCTAATA AAACTCAGTG CTGTGTTAAA | 720 |
| 50 | AAAAAAAAA AAAAAAGGGGG GCCCCNN | 757 |
| | (2) INFORMATION FOR SEQ ID NO: 95: | |
| 55 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 2394 base pairs(B) TYPE: nucleic acid | |
| 60 | (C) STRANDEDNESS: double (D) TOPOLOGY: linear | |

| (xı) | SEQUENCE | DESCRIPTION: | SEQ | ID | NO: | 95: |
|------|----------|--------------|-----|----|-----|-----|
| | | | | | | |

| 5 | GGCACGAGCA | CTCCTGCACT | TCCCCACCCC | CACGACCGAA | CCTGGCTTCG | CTAACGCCCT | 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| 3 | CCCAGCTCCC | TCGGGCCTGA | CTTCCGGTTT | CCTCGCGCGT | CCCTGGCGCC | GAGCCGCGGA | 120 |
| | CAGCAGCCCC | TTTTCCGGCT | GAGAGCTCAT | CCACACTTCC | AATCACTTTC | CGGAGTGCTT | 180 |
| 10 | CCCCTCCCTC | CGGCCCGTGC | TGGTCCCGAC | GCCGGCCTG | GGTCTCGCGC | GCGTATTGCT | 240 |
| | GGGTAACGGG | CCTTCTCYCG | CGTCGGCCCG | GCCCTCCTG | CCTCGGCTCG | TCCCTCCTTC | 300 |
| 15 | CAGAACGTCC | CGGGCTCCTG | CCGAGTCAGA | AGAAATGGGA | CTCCCTCCGC | GACGTGCCCG | 360 |
| 13 | GAGCAGCTCC | CTTCGCTGTG | GAAGCGGCGG | TGTCTTCGAA | GAAACCGGAA | GCCCGTGGTG | 420 |
| | ACCCCTGGCG | ACCCGGTTTG | TTTTCGGTCC | GTTTCCAAAC | ACTAAGGAAT | CGAAACTCGG | 480 |
| 20 | CGCCTTGGG | GGCGGCCCTA | CGTAGCCTGG | CTTCTGGTTG | TCATGGATGC | ACTGGTAGAA | 540 |
| | GATGATATCT | GTATTCTGAA | TCATGAAAAA | GCCCATAAGA | GAGATACAGT | GACTCCAGTT | 600 |
| 25 | TCAATATATT | CAGGAGATGA | ATCTGTTGCT | TCCCATTTTG | CTCTTGTCAC | TGCATATGAA | 660 |
| 23 | GACATCAAAA | AACGACTTAA | GGATTCAGAG | AAAGAGAACT | CTTTGTTAAA | GAAGAGAATA | 720 |
| | AGATTTTTGG | AAGAAAAGCT | AATAGCTCGA | TTTGAAGAAG | AAACAAGTTC | CGTGGGACGA | 780 |
| 30 | GAACAAGTAA | ATAAGGCCTA | TCATGCATAT | CGAGAGGTTT | GCATTGATAG | AGATAATTTG | 840 |
| | AAGAGCAAAC | TGGACAAAAT | GAATAAAGAC | AACTCTGAAT | CTTTGAAAGT | ATTGAATGAG | 900 |
| 35 | CAGCTACAAT | CTAAAGAAGT | AGAACTCCTC | CAGCTGAGGA | CAGAGGTGGA | AACTCAGCAG | 960 |
| 55 | GTGATGAGGA | ATTTAAATCC | ACCTTCATCA | AACTGGGAGG | TGGAAAAGTT | GAGCTGTGAC | 1020 |
| | CTGAAGATCC | ATGGTTTGGA | ACAAGAGCTG | GAACTGATGA | GGAAAGAATG | TAGCGATCTC | 1080 |
| 40 | AAAATAGAAC | TACAGAAAGC | CAAACAAACG | GATCCATATC | AGGAAGACAA | TCTGAAGAGC | 1140 |
| | AGAGATCTCC | AAAAACTAAG | CATTTCAAGT | GATAATATGC | AGCATGCATA | CTGGGAACTG | 1200 |
| 45 | AAGAGAGAAA | TGTCTAATTT | ACATCTGGTG | ACTCAAGTAC | AAGCTGAACT | ACTAAGAAAA | 1260 |
| 43 | CTGAAAACCT | CAACTGCAAT | CAAGAAAGCC | TGTGCCCCTG | TAGGATGCAG | TGAAGACCTT | 1320 |
| | GGAAGAGACA | GCACAAAACT | GCACTTGATG | AATTTTACTG | CAACATACAC | AAGACATCCC | 1380 |
| 50 | CCTCTCTTAC | CAAATGGCAA | AGCTCTTTGT | CATACCACAT | CTTCCCCTTT | ACCAGGAGAT | 1440 |
| | GTAAAGGTTT | TATCAGAGAA | AGCAATCCTC | CAATCATGGA | CAGACAATGA | GAGATCCATT | 1500 |
| 55 | CCTAATGATG | GTACATGCTT | TCAGGAACAC | AGTTCTTATG | GCAGAAATTC | TCTGGAAGAC | 1560 |
| JJ | AATTCCTGGG | TATTTCCAAG | TCCTCCTAAA | TCAAGTGAGA | CAGCATTTGG | GGAAACTAAA | 1620 |
| | ACTAAAACTT | TGCCTTTACC | CAACCTTCCA | CCACTGCATT | ACTTGGATCA | ACATAATCAG | 1680 |
| 60 | AACTGCCTTT | ATAAGAATTA | ATTTGGAAGA | GATTCACGAT | TTCACCATGA | GGACACTTAT | 1740 |

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| | CTCTTTCAGT | GGTCCTCCCA | AGAAATTATT | TAACAAACTG | AANGGAGATT | TTGATTAAAA | 1800 |
|----|------------|------------|------------|------------|-------------------|------------|------|
| 5 | TTTTGCAGAG | GTCTTCAGTA | TCTATATTTG | AACACACTGT | ACAATAGTAC | AAAAACCAAC | 1860 |
| 3 | ATAGTTGGTT | TTCTAGTATG | AAAGAGCACC | CTCTAGCTCC | ATATTCTAAG | AATCTGAAAT | 1920 |
| | ATGCTACTAT | ACTAATTAAT | AAGTAAACTT | AAGGTGTTTA | AAAAACTCTG | CCTTCTATAT | 1980 |
| 10 | TAATTGTAAA | ATTTTGCCTC | TCAGAAGAAT | GGAATTGGAG | ATTGTAGACG | TGGTTTTACA | 2040 |
| | AAATGTGAAA | TGTCTAAATA | TCTGTTCATA | AAAATAAAAG | GAAAACATGT | TTCTTCAAAT | 2100 |
| 15 | TGCATAATGG | AACAAATGGC | AATGTGAGTA | GGTTACATTT | CTGTTGTTAT | AATGCGTAAA | 2160 |
| 13 | GATATTGAAA | ATATAATGAA | ATAAAAGCAT | CTTAGGTTAT | ACCATCTTTA | TATGCTATTG | 2220 |
| | CGTTTCAATA | TTTAAGATTT | AAAGTGATTT | TTTGGTCACA | GTGTTTTGTT | GATAAAATTT | 2280 |
| 20 | TTTTAGAATT | GAAGTTTGAA | TTCTAAGACT | TGAAACAACC | TGATCACTGA | AGCCAACTTT | 2340 |
| | GTCCCAGCAC | ATTCCTTAAG | TCCTAATTGG | GGAAAAAAA | ААААААА АС | TCGA | 2394 |

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(2) INFORMATION FOR SEQ ID NO: 96:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 672 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NC: 96:

| AGTGCTCTGT | TGCCCAGGCT | GGAGTGCGTT | AGTGTAATGT | CAGTCCACTG | CAACCTCCAC | 60 |
|------------|------------|------------|------------|------------|------------|-----|
| CCCCAGGTTC | AAGCAATTCT | CATGCCTCAG | CCTCCCAAGT | AGCTGAAATT | ACTGGCATGC | 120 |
| ACCACCACAC | CCAGCTGATG | TTATTTATTT | TATTTATATA | TTTATTTATT | TTAGGTGTTT | 180 |
| TTTTTTTTT | TTTTTGAGAC | GGAGTCTTGC | TCTGTTGCCC | TGGGTGTGGT | TACGTGGRAT | 240 |
| TACCATYCTG | GGTGACTCAC | TGAAATGTAC | TCMCAGTGAG | TCATGCCTTC | MAATGACATC | 300 |
| TCAAGTTCTG | CCTGCTTGGA | GATACATCTG | GGGATCTTAA | GGGGTGAGGG | ACTACTCAAC | 360 |
| AAGAAGGAAT | TTAGCCTGTC | TTTTTAAATA | AACGCCATTT | CTTTTTCCTA | KAAAAATGGG | 420 |
| AAATTCTTCA | ATTCTCTAAT | ACAGGGACAC | TGAGATAACA | AAGAGGAAAG | TGTCTGGTTG | 480 |
| GAGGTTGGGA | RGCCACCCTG | GGGTCTCTCC | TACAAAAATG | GAAAAGAAAA | GAACGGTGAR | 540 |
| AAATCMAGCA | AAGCACAARA | AAKTTTCCCT | TTGCTAAAAG | GGAAAAGATG | CCCCMCAATG | 600 |
| CCCATAAACA | TGAACTGGGG | ATAAGGAGGA | RAATGTCTCT | YCTTGGCACC | CCCAAACAAA | 660 |
| CGTTAATTAC | cc | | | | | 672 |

BNSDOCID: <WO___9842738A1_IA>

| (2) | INFORMATION | FOR | SEQ | ID | NO: | 97: |
|-----|-------------|-----|-----|----|-----|-----|
|-----|-------------|-----|-----|----|-----|-----|

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1419 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

10

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

| 15 | TAAGAACAGA | ACAGCAAGTA | TGAACCACAT | GGAACTTAAA | ACATATGGGT | GTGAAGTCCA | 60 |
|-----------|------------|------------|------------|------------|------------|------------|------|
| 13 | CTTATGTAGA | CAAAACTTAT | AATTTCCAAA | CTGTTGTCTA | GTATACAGTG | ATCAGTTGCT | 120 |
| | CTCTGTTCAA | GTCATTCCAC | ACATTTCCCT | ATTTTAGGCT | ATTATAATAT | AGAAAGAAAA | 180 |
| 20 | TGGGAAGCAT | TAGTTGGAGC | TAGAAAATGA | ACTGTATATT | ATTGCTATAT | TTGCTAATAC | 240 |
| | CAACTATTTC | AATAAGTGTT | GTACCATATG | TAGCATTAAA | TATAAAATAC | ATAAAAGAAT | 300 |
| 25 | GTACAGAAAA | TAGCTTTTAT | TGAGTAATAT | TACATTTCAT | TTATACTGTA | GCAATATATT | 360 |
| 23 | TGTAGGTATA | CTCTGTAAGG | GCTTTAAATA | AAAGAGGTCC | ATTAATACTT | CCTTATAAAA | 420 |
| | ATTCTAGTCT | GTTTCATTAC | TGCCCAGATG | TTTTAGAGAT | AAATATTTAT | GCAGAAGGTA | 480 |
| 30 | TTTKGAAAG | TCYCCYTTTG | TCTGATAGAG | TTTAACNAGA | TATTTAAATT | TAGTGCYCNA | 540 |
| | GAAATCCCAC | AAGTCACGGT | CTAAACACAC | TTAGAATACT | ACAGCATAAA | TCTGTTAGCA | 600 |
| 35 | TTANTTGCCA | AATAAGACAG | TTGGGATCCC | AAACCCCAAG | TCCTTGAGCA | ATGTTTTTCC | 660 |
| 33 | TCAAAAAĞCT | GCTATNCCAA | TGATATAGGA | AAAWACATTG | TGTTTTCCTA | AACACACTTT | 720 |
| | TCTTTTTAAA | TGTGCTTCAT | TGTTTGATTT | GGTCCTGCCT | AAATTTCACA | AGCTAGGCCA | 780 |
| 40 | ATGAAGGCTG | AATCAAAGAC | ATTTCATCCA | CCAATATCAT | GTGTAGATAT | TATGTATAGA | 840 |
| | ATAAAATAAA | AATTATGGCT | CTAACTTCTG | TGTTGCTGTT | TATCTTGTTA | TTTTTCGGCG | 900 |
| 45 | TTATACTAAT | GNGTTTATTG | AGAGCATTTT | ACCTTCCAGA | CTTCTCATGG | CTAACTTTTG | 960 |
| 73 | GTCTGWATTT | TGSTCCTTAG | ATGKGAATAT | TTCTTATTAG | TYTGCTYCCT | GCWACGCAAT | 1020 |
| | GACTGCATTT | CTATCATTTC | TCAGTTTGTT | AGWATATGTG | GATAGTATTC | TACTGTATAA | 1080 |
| 50 | ATGATTGCAA | AGTTTATCAA | AAACAAATTA | TTATATGTAG | CTTTTCTACA | GTGCTTTGCT | 1140 |
| | AAACCATGTA | GTACTAGTTA | AGTSTTCCTT | GAAAATAAAG | ATACACTCTT | ATAGGGGACA | 1200 |
| 55 | GTTCCTGTTC | ACTCCCAGGA | AACTTTTTTA | AAAGATGACA | CTGAATGTTT | ATTGCACTTT | 1260 |
| <i>33</i> | AGTGCAGTGA | AGTGGCAATA | AAACCTAACA | TGAATCAAGG | TTGTTTATGG | CAGATGCATG | 1320 |
| | TGTTGCTTTA | CAGAGTTTAG | CAAAAGCTCT | TAATTTTATG | TCATACTGTA | TTCTACTGAA | 1380 |
| 60 | TAATAAAGCT | AACATTATTC | AATAATAAA | TGGAAAAAA | | | 1419 |

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5 (2) INFORMATION FOR SEQ ID NO: 98:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1487 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

| | , , | ~ | | | | | |
|----|------------|------------|------------|------------|------------|------------|------|
| 15 | GCGACCGCGC | CCCTTTCAGC | TAGCTCGCTC | GCTCGCTCTG | CTTCCCTGCT | GCCGGCTGCG | 60 |
| | CATGGCKWTG | GCGTTGGCGG | CGCTGGCGGC | GGTCGAGCCG | GCCTGCGCAG | CCGGTACCAG | 120 |
| 20 | CAGTTGCAGA | ATGAAGAAGA | GTCTGGAGAA | CCTGAACAGG | CTGCAGGTGA | TGCTCCTCCA | 180 |
| 20 | CCTTACAGCA | GCATTTCTGC | AGAGAGCGCA | GTTTTCCACC | TATTTCCCTG | GATATTTTGA | 240 |
| | TGGTCAGTAC | TGGCTCTGGT | GGGTGTTCCT | TGTTTTAGGC | TTTCTCCTGT | TTCTCAGAGG | 300 |
| 25 | ATTTATCAAT | TATGCAAAAG | TTCGGAAGAT | GCCAGAAACT | TTCTCAAATC | TCCCCAGGAC | 360 |
| | CAGAGTTCTC | TTTATTTATT | AAAGATGTTT | TCTGGCAAAG | GCCTTCCTGC | ATTTATGAAT | 420 |
| 30 | TCTCTCTCAA | GAAGCAAGAG | AACACCTGCA | GGAAGTGAAT | CAAGATGCAG | AACACAGAGG | 480 |
| 30 | AATAATCACC | TGCTTTAAAA | AAATAAAGTA | CTGTTGAAAA | GATCATTTCT | CTCTATTTGT | 540 |
| | TCCTAGGTGT | AATTTTAA | TAGTTAATGC | AGAATTCTGT | AATCATTGAA | TCATTAGTGG | 600 |
| 35 | TTAATGTTTG | AAAAAGCTCT | TGCAATCAAG | TCTGTGATGT | ATTAATAATG | CCTTATATAT | 660 |
| | TGTTTGTAGT | CATTTTAAGT | AGCATGAGCC | ATGTCCCTGT | AGTCGGTAGG | GGGCAGTCTT | 720 |
| 40 | GCTTTATTCA | TCCTCCATCT | CAAAATGAAC | TTGGAATTAA | ATATTGTAAG | ATATGTATAA | 780 |
| 40 | TGCTGGCCAT | TTTAAAGGGG | TTTTCTCAAA | AGTTAAACTT | TTGTTATGAC | TGTGTTTTTG | 840 |
| | CACATAATCC | ATATTTGCTG | TTCAAGTTAA | TCTAGAAATT | TATTCAATTC | TGTATGAACA | 900 |
| 45 | CCTGGAAGCA | AAATCATAGT | GCAAAAATAC | ATTTAAGGTG | TGGTCAAAAA | TAAGTCTTTA | 960 |
| | ATTGGTAAAT | AATAAGCATT | AATTTTTTAT | AGCCTGTATT | CACAATTCTG | CGGTACCTTA | 1020 |
| 50 | TTGTACCTAA | GGGATTCTAA | AGGTGTTGTC | ACTGTATAAA | ACAGAAAGCA | CTAGGATACA | 1080 |
| 30 | AATGAAGCTT | AATTACTAAA | ATGTAATTCT | TGACACTCTT | TCTATAATTA | GCGTTCTTCA | 1140 |
| | CCCCCACCC | CACCCCCACC | CCCCTTATTT | TCCTTTTGTC | TCCTGGTGAT | TAGGCCAAAG | 1200 |
| 55 | TCTGGGAGTA | AGGAGAGGAT | TAGGTACTTA | GGAGCAAAGA | AAGAAGTAGC | TTGGAACTTT | 1260 |
| | TGAGATGATC | CCTAACATAC | TGTACTACTI | GCTTTTACAA | TGTGTTAGCA | GAAACCAGTG | 1320 |
| 60 | GGTTATAATG | TAGAATGATG | TGCTTTCTGC | CCAAGTGGTA | ATTCATCTTG | GTTTGCTATG | 1380 |
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(2) INFORMATION FOR SEQ ID NO: 99:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1653 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

GCGACCGCGC CCTTCAGCTA GCTCGCTCGC TCGCTCTGCT TCCCTGCTGC CGGCTGCGCA

20 TGGCTTNGGC GTTGGCGGCG CTGGCGGCGG CTCGAGCCGC CTGCGSAGCC GGTACCAGCA 120 GTTGCAGAAT GAAGAAGACT CTGGAGAACC TGAACAGGCT GCAGGTGATG CTCCTCCACC 180 TTACAGCAGC ATTTCTGCAG AGAGCGCACA TNATTTTGAC TACAAGGATG AGTCTGGGTT 240 25 TCCAAAGCCC CCATCTTACA ATGTAGCTAC AACACTGCCC AGTTATGATG AAGCGGAGAG 300 GACCAAGGCT GAAGCTACTA TCCCTTTGGT TCCTGGGAGA GATGAGGATT TTGTGGGTCG 360 30 GGATGATTTT GATGATGCTG ACCAGCTGAG GATAGGAAAT GATGGGATTT TCATGTTAAC 420 TTTTTTCATG GCATTCCTCT TTAACTGGAT TGGGTTTTTC CTGTCTTTTT GCCTGACCAC 480 TTCAGCTGCA GGAAGGTATG GGGCCATTTC AGGATTTGGT CTCTCTAA TTAAATGGAT 540 35 CCTGATTGTC AGGTTTTCCA CCTATTTCCC TGCATTTATG AATTCTCTCT CAAGAAGCAA 600 GAGAACACCT GCAGGAAGTG AATCAAGATG CAGAACACAG AGGAATAATC ACCTGCTTTA 660 40 AAAAAATAAA GTACTGTTGA AAAGATCATT TCTCTCTATT TGTTCCTAGG TGTAAAATTT 720 TAATAGTTAA TGCAGAATTC TGTAATCATT GAATCATTAG TGGTTAATGT TTGAAAAAGC 780 TCTTGCAATC AAGTCTGTGA TGTATTAATA ATGCCTTATA TATTGTTTGT AGTCATTTTA 840 45 AGTAGCATGA GCCATGTCCC TGTAGTCGGT AGGGGGCAGT CTTGCTTTAT TCATCCTCCA 900 TCTCAAAATG AACTTGGAAT TAAATATTGT AAGATATGTA TAATGCTGGC CATTTTAAAG 960 50 GGGTTTTCTC AAAAGTTAAA CTTTTGTTAT GACTGTGTTT TTGCACATAA TCCATATTTG 1020 CTGTTCAAGT TAATCTAGAA ATTTATTCAA TTCTGTATGA ACACCTGGAA GCAAAATCAT 1080 AGTGCAAAAA TACATTTAAG GTGTGGTCAA AAATAAGTCT TTAATTGGTA AATAATAAGC 1140 55 ATTAATTTT TATAGCCTGT ATTCACAATT CTGCGGTACC TTATTGTACC TAAGGGATTC 1200 TAAAGGTGTT GTCACTGTAT AAAACAGAAA GCACTAGGAT ACAAATGAAG CTTAATTACT 1260 60 AAAATGTAAT TCTTGACACT CTTTCTATAA TTAGCGTTCT TCACCCCCAC CCCCACCCCC 1320

| | ACCCCCTTA | TTTTCCTTTT | GTCTCCTGGT | GATTAGGCCA | AAGTCTGGGA | GTAAGGAGAG | 1380 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | GATTAGGTAC | TTAGGAGCAA | AGAAAGAAGT | AGCTTGGAAC | TTTTGAGATG | ATCCCTAACA | 1440 |
| 3 | TACTGTACTA | CTTGCTTTTA | CAATGTGTTA | GCAGAAACCA | GTGGGTTATA | ATGTAGAATG | 1500 |
| | ATGTGCTTTC | TGCCCAAGTG | GTAATTCATC | TTGGTTTGCT | ATGTTAAAAC | TGTAAATACA | 1560 |
| 10 | ACAGAACATT | AATAAATATC | TCTTGTGTAG | CACCTTTTAW | ААААААААА | AAAAAAAA | 1620 |
| | АААААААА | AAAAANCCCG | GGGGGGGCC | CCN | | | 1653 |

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(2) INFORMATION FOR SEQ ID NO: 100:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1145 base pairs

(B) TYPE: nucleic acid(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

| TTTTTTTTT T | TATATATATAT | TTGACTGAAC | TAAGTGGCTT | TTTTATTAGA | GAAAGCCAGA | 60 |
|--------------|-------------|------------|------------|------------|------------|------|
| ATTACAAAAG A | CTTCCCTTT | TCTTGGGGTA | TGGCTGTCTC | AGCACAATAC | TCAACATAAC | 120 |
| TGCAGAACTG A | TGTGGCTCA | GGCACCCTGG | TTTTAATTCC | TTGAGGATCT | GGCAATTGGC | 180 |
| TTACGCAAAA G | GTCACCATT | TGAGGTCCTG | CCTTACTAAT | TATGTGCTGC | CCAACAACTA | 240 |
| AATTTGTAAT T | TGTTTTCT | CTAGTTTGAG | CAGGGTCTGA | ATTTTTCAT | TTATTTCCTT | 300 |
| TTTTGCCAGC A | GACAGACTT | GAGTCTGTAA | AGACAAGCAA | ATACACTGAC | AGAAGTTTAC | 360 |
| CATAGTTTCT A | AAATGTAAA | AAAGAAAACC | CCCAAAAGAC | TCAAGAAAAT | TAGACCACAA | 420 |
| ATTITGCATT G | STTCATTGTA | GCACTATTGG | ТААТАААТА | ACAAATGTTT | GTGCATTTTT | 480 |
| ATGTGAAGAT C | CCTTCTCGTA | TTTCATTTGG | AAAGATGAGC | AAGAGGTCTG | CTTCCTTCAT | 540 |
| TTTACTTCCC C | CTTCTGTTTT | TGAAAGGCAG | TTTCGCCAAG | CTTAATGCAA | GAATATCTGA | 600 |
| CTGTTTAGAA G | GAAAGATATT | GCCACAATCT | CTGGATGGTT | TTCCAGGGTT | GTGTTATTAC | 660 |
| TGAGCTTCAT C | CTTTCCAGAA | TGAGCAAAAC | ACTGTCCAGT | CTTTGTTACG | ATTTTGTAAT | 720 |
| AAATGTGTAC A | ATTTTTTTA | AATTTTTGGA | CATCACATGA | ATAAAGGTAT | GTATGTACGA | 780 |
| ATGTGTATAT A | ATATATATA | TGACATCTAT | TTTGGAAAAT | GTTTGCCCTG | CTGTACCTCA | 840 |
| TTTTTAGGAG (| GTGTGCATGG | ATGCAATATA | TGAAAATGGG | ACATTCTGGA | ACTGCTGGTC | 900 |
| AGGGGACTTT (| GTCGCCCTGT | GCACTAAAAG | GGCCAGATTT | TCAGCAGCCA | AGGACATCCA | 960 |
| TACCCAAGTG A | AATGTGATGG | GACTTAAAAG | AAGTGAACTG | AGACAATTCA | CTCTGGCTGT | 1020 |

| | TTGAACAGCA GCGTTTCATA GGAAGAGAAA AAAAGATCAA TCTTGTATTT TCTGACCACA | 1080 |
|----|---|------|
| | TAAAGGCTTC TTCTCTTTGT AATAAAGTAG AAAAGCTCTC CTCAAAAAAA AAAAAAAAA | 1140 |
| 5. | AAAAA | 1145 |
| | | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 101: | |
| 15 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 734 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double(D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101: | |
| 20 | TACCCGGCGG ATTCCAGGAA GGTAAATTTA GTCCTATAAT TTTCAGCTTA ATTATAAACA | 60 |
| | AAGGAACAAA TAAGTGGAAG GGCAGCTATT ACCATTCGCT TAGTCAAAAC ATTCGGTTAC | 120 |
| 25 | TGCCCTTTAA TACACTCCTA TCATCAGCAC TTCCACCATG TATTACAAGT CTTGACCCAT | 180 |
| 23 | CCCTGTCGTA ACTCCAGTAA AAGTTACTGT TACTAGAAAA TTTTTTATCAA TTAACTGACA | 240 |
| | AATAGTTTCT TTTTAAAGTA GTTTCTTCCA TCTTTATTCT GACTAGCTTC CAAAATGTGT | 300 |
| 30 | TCCCTTTTTG AATCGAGGTT TTTTTGTTTT GTTTTGTTTT | 360 |
| | TGTGCTTCTA TTGCTTTTTT GTGTTTTGTT AAGCATGTCC CTTGGCCCAA ATGGAAGAGG | 420 |
| 35 | AAATGTTTAA TTAATGCTTT TTAGTTTAAA TAAATTGAAT CATTTATAAT AATCAGTGTT | 480 |
| 33 | AACAATTTAG TGACCCTTGG TAGGTTAAAG GTTGCATTAT TTATACTTGA GATTTTTTC | 540 |
| | CCCTAACTAT TCTGTTTTTT GTACTTTAAA ACTATGGGGG AAATATCACT GGTCTGTCAA | 600 |
| 40 | GAAACAGCAG TAATTATTAC TGAGTTAAAT TGAAAAGTCC AGTGGACCAG GCATTTCTTA | 660 |
| | TATAAATAAA ATTGGTGGTA CTAATGTGAA AAAAAAAAAA | 720 |
| 45 | CCGGTACCCT ATTA | 734 |
| 43 | | |
| 50 | (2) INFORMATION FOR SEQ ID NO: 102: | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 713 base pairs | |
| | (B) TYPE: nucleic acid (C) STRANDEDNESS: double | |
| 55 | (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102: | |
| 60 | CCGCGGGAAC GCTGTCCTGG CTGCCGNCAC CCGAACAGCC TGTCCTGGTG CCCCGGCTCC | 60 |

| | CTGCCCCGCG | CCCAGTCATG | ACCCTGCGCC | CCTCACTCCT | CCCGCTCCAT | CTGCTGCTGC | 120 |
|----|------------|------------|------------|------------|------------|------------|-----|
| | TGCTGCTGCT | CAGTGCGGCG | GTGTGCCGGG | CTGAGGCTGG | GCTCGAAACC | GAAAGTCCCG | 180 |
| 5 | TCCGGACCCT | CCAAGTGGAG | ACCCTGGTGG | AGCCCCCAGA | ACCATGTGCC | GAGCCCGCTG | 240 |
| | CTTTTGGAGA | CACGCTTCAC | ATACACTACA | CGGGAAGCTT | GGTAGATGGA | CGTATTATTG | 300 |
| 10 | ACACCTCCCT | GACCAGAGAC | CCTCTGGTTA | TAGAACTTGG | CCAAAAGCAG | GTGATTCCAG | 360 |
| 10 | GTCTGGAGCA | GAGTCTTCTC | GACATGTGTG | TGGGAGAGAA | GCGAAGGGCA | ATCATTCCTT | 420 |
| | CTCACTTGGC | CTATGGAAAA | CGGGGATTTC | CACCATCTGT | CCCAGCGGAT | GCAGTGGTGC | 480 |
| 15 | AGTATGACGT | GGAGCTGATT | GCACTAATCC | GAGCCAACTA | CTGGCTAAAG | CTGGTGAAGG | 540 |
| | GCATTTTGCC | TCTGGTAGGG | ATGGCCATGG | TGCCACCCTC | CTGGGCCTCA | TTGGGTATCA | 600 |
| 20 | CCTATACAGA | AAGGCCAATA | GACCCAAAGT | CTCCAAAAAG | AAGCTCAAGG | AAGAGAAACG | 660 |
| 20 | AAACAAGAGC | AAAAAGAAAT | ААТАААТАА | AAATTTTAAA | AAACTTAAAA | AAA | 713 |

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(2) INFORMATION FOR SEQ ID NO: 103:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1080 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

35 CCGATGTGGA CATCATCCTG TCTATCCCCA TGTTCCTGCG CCTGTACCTG ATCGCCCGAG 60 TCATGCTGCT GCACAGAAGC TCTTCACCGA TGCCTCGTCC CGCAGCATCG GGGCCCTCAA 120 CAAGATCAAC TTCAACACCC GCTTTGTCAT GAAGACGCTC ATGACCATCT GCCCTGGCAC 40 180 TGTGCTGCTC GTGTTCAGCA TCTCTCTGTG GATCATTGCT GCCTGGACCG TCCGTGTCTG 240 TGAAAGTCCT GAATCACCAG CCCAGCCTTC TGGCTCATCA CTTCCTGCTT GGTACCATGA 300 45 CCAGCAGGAC GTAACTAGTA ACTITCTGGG TGCCATGTGG CTCATCTCCA TCACATTCCT 360 TTCCATTGGT TATGGGGACA TGGTGCCCCA CACATACTGT GGGAAAGGTG TCTGTCTCCT 420 50 CACTGGCATC ATGGGTGCAG GCTGCACTGC CCTTGTGGTG GCCGTGGTGG CCCGAAAGCT 480 GGAACTCACC AAAGCGGAGA AGCACGTTCA TAANTTCATG ATGGACACTC AGCTCACCAA 540 GCGGATCAAG AATGYTGCAG CCAATGTCCT TSGGGAAACA TGGTTAATCT ATAAACACAC 600 55 AAAGYTGYTA AAGAAGATTG ACCATGCCAA AGTGAGGAAC ACCAGAGGAA GTTCYTCCAA 660 GTATCCACCA GTTGAGGAGC GTCAAGATGG AACAGAGGAA GCTGAGTGAC CAAGCCAACA 720 780 60 NTCTGGTGGA CCTTTCCAAG ATGCAGAATG TCMTGTATGA CTTAATCACA GAACTCAATG

| | ACCGGAGCGA AGACCTGGAG AAGCAGATTG GCAGCCTGGA GTCGAAGCTG GAGCATCTCA | 840 |
|----|---|-------------|
| 5 | CCGCCAGCTT CAACTCCCTG CCGCTGCTCA TCGCCGACAC CCTGCGCCAG CAGCAGCAGC | 900 |
| 3 | AGCTCCTGTC TGCCATCATC GAGGCCCGGG GTGTCAGCGT GGCAGTGGGC ACCACCCACA | 960 |
| | CCCCAATCTC CGATAGCCCC ATTGGGGTCA GCTCCACCTC CTTCCCGACC CCGTACACAA | 1020 |
| 10 | GTTCAAGCAG TTGCTAAATA AATCTCCCCA CTCCAGAAGC ATTAAAAAAA AAAAAAAAAA | 1080 |
| | | |
| 15 | (a) THEODINATION FOR CEO TO NO. 104. | |
| 13 | (2) INFORMATION FOR SEQ ID NO: 104: | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 489 base pairs | |
| 20 | (B) TYPE: nucleic acid (C) STRANDEDNESS: double | |
| | (D) TOPOLOGY: linear | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104: | |
| 25 | GGCACGAGAG GCTTTGAAGC ATTTTTGTCT GTGCTCCCTG ATCTTCAGGT CACCACCATG | 60 |
| | AAGTTCTTAG CAGTCCTGGT ACTCTTGGGA GTTTCCATCT TTCTGGTCTC TGCCCAGAAT | 120 |
| 30 | CCGACAACAG CTGCTCCAGC TGACACGTAT CCAGCTACTG GTCCTGCTGA TGATGAAGCC | 180 |
| 50 | CCTGATGCTG AAACCACTGC TGCTGCAACC ACTGCGACCA CTGCTGCTCC TACCACTGCA | 240 |
| | ACCACCGCTG CTTCTACCAC TGCTCGTAAA GACATTCCAG TTTTACCCAA ATGGGTTGGG | 300 |
| 35 | GATCTCCCGA ATGGTAGAGT GTGTCCCTGA GATGGAATCA GCTTGAGTCT TCTGCAATTG | 360 |
| | GTCACAACTA TTCATGCTTC CTGTGATTTC ATCCAACTAC TTACCTTGCC TACGATATCC | 420 |
| 40 | CCTTTATCTC TAATCAGTTT ATTTTCTTTC AAATAAAAA TAACTATGAG CAACAAAAAA | 480 |
| 10 | ААААААА | 4 89 |
| | | |
| 45 | (2) INFORMATION FOR SEQ ID NO: 105: | |
| | - W. | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 640 base pairs | |
| 50 | (B) TYPE: nucleic acid (C) STRANDEDNESS: double | |
| | (D) TOPOLOGY: linear | |
| 55 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105: | |
| 55 | GCGGTCGCCG CTGTTGTTGT GGTCCCCATG GAGCTGCCGT AGCGGACCCA GCACAGCCAG | 60 |
| | GAGCGTCCGG GATGAGCTCA GCCGCGGCCG ACCACTGGGC GTGGTTGCTG GTGCTCAGCT | 120 |
| 60 | TCGTGTTTGG ATGCAATGTT CTTAGGATCC TCCTCCCGTC CTTCTCATCC TTCATGTCCA | 180 |

| | GGGTGCTGCA | GAAGGACGCG | GAGCAGGAGT | CACAGATGAG | AGCGGAGATC | CAGGACATGA | 240 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 5 | AGCAGGAGCT | CTCCACAGTC | AACATGATGG | ACGAGTTTGC | CAGATATGCC | AGGCTGGAAA | 300 |
| 3 | GAAAGATCAA | CAAGATGACG | GATAAGCTCA | AAACCCATGT | GAAAGCTCGG | ACAGCTCAAT | 360 |
| | TAGCCAAGAT | AAAATGGGTG | ATAAGTGTCG | CTTTCTACGT | ATTGCAGGCT | GCCCTGATGA | 420 |
| 10 | TCTCACTCAT | TTGGAAGTAT | TATTCTGTCC | CTGTGGCTGT | CGTGCCGAGT | AAATGGATAA | 480 |
| | CCCTYTAGAC | CGCCTGGTAG | CCTTTCCYAY | TAGAGTAGCA | GGTGGTGTTG | GAATTACTGT | 540 |
| 15 | TGGATTTART | CTGTACAAAT | TGTCCTATTG | TGCTTCACCG | TYCASTGAAC | AGGAGGTGGT | 600 |
| 15 | ACAGCCGGAG | TTAAAAACGG | TTTCCNTTCC | AGTTTAAAAT | | | 640 |

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(2) INFORMATION FOR SEQ ID NO: 106:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1529 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

GGGCACNAGA TGGAGCTGCC GTAGCGGACC CAGCACAGCC AGGAGCGTCC GGGATGAGCT 60 CAGCCGCGGC CGACCACTGG GCGTGGTTGC TGGTGCTCAG CTTCGTGTTT GGATGCAATG 120 TTCTTAGGAT CCTCCTCCG TCCTTCTCAT CCTTCATGTC CAGGGTGCTG CAGAAGGACG 180 35 CGGACAGGAG TCACAGATGA GAGCGGAGAT CCAGGACATG AAGCAGGAGC TCTCCACAGT 240 CAACATGATG GACGAGTTTG CCAGATATGC CAGGCTGGAA AGAAAGATCA ACAAGATGAC 40 GGATAAGCTC AAAACCCATG TGAAAGCTCG GACAGCTCAA TTAGCCAAGA TAAAATGGGT 360 GATAAGTGTC GCTTTCTACG TATTGCAGGC TGCCCTGATG ATCTCACTCA TTTGGAAGTA 420 45 TTATTCTGTC CCTGTGGCTG TCGTGCCGAG TAAATGGATA ACCCCTCTAG ACCGCCTGGT 480 AGCCTTTCCT ACTAGAGTAG CAGGTGGTGT TGGAATTACC TGTTGGATTT TAGTCTGTAA 540 CAAAGTTGTC GCTATTGTGC TTCATCCGTT CAGCTGAACA GGAGGATGGA TACAGCCGCG 600 50 AGTAAAAAA CGGATTTCCT CTTCCTAGCT TAAAATCTGA TTTACACTGT TTTGTTTTTT 660 AAGAAACAAA AGTGCATAGT TTAGATTTTT TTTTTGTTGA ATATGTTTGT TCTTGGACTT 720 780 55 TATGAGATAG TCTTATAAGA ATCACGATTT TCTACACCTG TCATTGAGCC AAGAAAGTCC AGTTTATGAC ACGTATGTAC TAGTGAACAC CGTCCTCGAT CTGTACGAAA TGTGAAATGT 840 TTAGGGACAT CTCCATGCTG TCACTTGTGA TTTGCCCTCT TATGTATTTT GGTCATATTG 900 60

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| | CCAACTGGAA | AGTCAAAATT | TTCTAACAAC | TTTAAGTAAG | TTCTTTGAAG | ACTTAGTGCT | 960 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GTTTTTAATC | CAGTTTAGAA | AGTAACTTAA | TTTTAATACC | RCTACTAAAA | ATTCGAAAAT | 1020 |
| 5 | TTCTTCTTTA | ATCACATTCA | ATATGGTTAA | AAGAACAACA | CTAATTGACA | TTGCGTGGGC | 1080 |
| | TTTTTCTCCC | TTTGTTTAAA | ATGTCATTTG | TTGAGCAAGA | GTTGTATAGT | ATTATCTACT | 1140 |
| 10 | TACTTGAGGC | TGTTAATTTT | TCATTACAGT | GTTTTGTAAA | TGTATCCACG | AGACCATGAT | 1200 |
| 10 | GCATTGTTTT | GTGCTCAACT | TGTGTTTTGT | ATTTAAAGCA | TTTTGAATGA | AGTGTATTTT | 1260 |
| | ATAAGCATTT | AATATTTATG | CTCTTTAGAA | TGGAACACAG | AAAACAAACC | TTATAAGTCC | 1320 |
| 15 | TGATTAATCT | GAACCAATAA | CCTGTGTGGC | CTACAAAGTA | TAATTCTATT | AAATGTTCCT | 1380 |
| | TAAAACACTT | TTTTCTAATT | AAAATCTTTG | CAAATGCTTG | TGTAACTTCC | TGCCTTACAG | 1440 |
| 20 | CTACTTGTTT | GCTGTGAGCC | ACCCGCAACT | GACAAGTGGC | TGTTAACTGA | GTCACCATAT | 1500 |
| | CCCAGTAAAG | CTGAATTTTC | ТСАСТАААА | | | | 1529 |

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(2) INFORMATION FOR SEQ ID NO: 107:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2435 base pairs(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107: 35

ATGAAGGGTC GTTGGTGGGA AAGATGGCGG CGACTCTGGG ACCCCTTGGT CGTGGCAGCA 60 GTGGCGRCGA TGTTTGTCGG CTCGGGATGG GTCCAGGATG TTACTCCTTC TTCTTTTGTT 120 40 GGGTCTGGG CAGGGGCCAC AGCAAGTCGG GGCGGGTCAA ACGTTCGAGT ACTTGAAACG 180 GGAGCACTCG CTGTCGAAGC CCTACCAGGG TGTGGGCACA GGCAGTTCCT CACTGTGGAA 240 TCTGATGGGC AATGCCATGG TGATGACCCA GTATATCCGC CTTACCCCAG ATATGCAAAG 300 45 TAAACAGGGT GCCTTGTGGA ACCGGGTGCC ATGTTTCCTG AGAGACTGGG AGTTGCAGGT 360 GCACTTCAAA ATCCATGGAC AAGGAAAGAA GAATCTGCAT GGGGATGGCT TGGCAATCTG 420 50 GTACACAAAG GRWTCGGATG CAGCCAGGGC CTGTNTTTGG GAAACATGGA CAAATTTGTG 480 GGGCTGGGAG TATTTGTAGA CACCTACCCC AATGAGGAGA AGCAGCAAGA GCGGGTATTC 540 CCCTRCMTCT CAGCCATGGT GAACAACGGC TCCCTCAGCT ATGATCATGA GCGGGATGGG 600 55 CGGCCTACAG AGCTGGGAGG CTGCASAGCC ATTGTCCGCA ATCTTCATTA CGACACCTTC 660 CTGGTGATTC GCTACGTCAA GAGGCATTTR ACGATAATGA TGGATATTGA TGGCAAGCAT 720 60 GAGTGGAGGG ACTGCATTGA AGTGCCCGGA GTCCGCCTGC CCCGCGGCTA CTACTTCGGC 780

| | ACCTCCTCCA | TCACTGGGGA | TCTCTCAGAT | AATCATGATG | TCATTTCCTT | GAAGTTGTTT | 840 |
|------------|------------|------------|------------|------------|------------|------------|------|
| 5 | GAACTGACAG | TGGAGAGAAC | CCCAGAAGAG | GAAAAGCTCC | ATCGAGATGT | GTTCTTGCCC | 900 |
| 5 | TCAGTGGACA | ATATGAAGCT | GCCTGAGATG | ACAGCTCCAC | TGCCGCCCCT | GAGTGGCCTG | 960 |
| | GCCCTCTTCC | TCATCGTCTT | TTTCTCCCTG | GGTGTTTTCT | GTATTTGCCA | TAGTCATTGG | 1020 |
| 10 | TATCATACTC | TACAACAAAT | GGCAGGAACA | GAGCCGAAAG | CGCTTCTACT | GAGCCCTCCT | 1080 |
| | GCTGCCACCA | CTTTTGTGAC | TGTCACCCAT | GAGGTATGGA | AGGAGCAGGC | ACTGGCCTGA | 1140 |
| 15 | GCATGCAGCC | TGGAGAGTGT | TCTTGTCTCT | AGCAGCTGGT | TGGGGACTAT | ATTCTGTCAC | 1200 |
| 13 | TGGAGTTTTG | AATGCAGGGA | CCCCGCATTC | CCATGGTTGT | GCATGGGGAC | ATCTAACTCT | 1260 |
| | GGTCTGGGAA | GCCACCCACC | CCAGGGCAAT | GCTGCTGTGA | TGTGCCTTTC | CCTGCAGTCC | 1320 |
| 20 | TTCCATGTGG | GAGCAGAGGT | GTGAAGAGAA | TTTACGTGGT | TGTGATGCCA | AAATCACAGA | 1380 |
| | ACAGAATTTC | ATAGCCCAGG | CTGCCGTGTT | GTTTGACTCA | GAAGGCCCTT | CTACTTCAGT | 1440 |
| 25 | TTTGAATCCA | CAAAGAATTA | AAAACTGGTA | ACACCACAGG | CTTTCTGACC | ATCCATTCGT | 1500 |
| 23 | TGGGTTTTGC | ATTTGACCCA | ACCCTCTGCC | TACCTGAGGA | GCTTTCTTTG | GAAACCAGGA | 1560 |
| | TGGAAACTTC | TTCCCTGCCT | TACCTTCCTT | TCACTCCATT | CATTGTCCTC | TCTGTGTGCA | 1620 |
| 30 | ACCTGAGCTG | GGAAAGGCAT | TTGGATGCCT | CTCTGTTGGG | GCCTGGGGCT | GCAGAACACA | 1680 |
| | CCTGCGTTTC | ACTGGCCTTC | ATTAGGTGGC | CCTAGGGAGA | TGGCTTTCTG | CTTTGGATCA | 1740 |
| 35 | CTGTTCCCTA | GCATGGGTCT | TGGGTCTATT | GGCATGTCCA | TGGCCTTCCC | AATCAAGTCT | 1800 |
| 33 | CTTCAGGCCC | TCAGTGAAGT | TTGGCTAAAG | GTTGGTGTAA | AAATCAAGAG | AAGCCTGGAA | 1860 |
| | GACATCATGG | ATGCCATGGA | TTAGCTGTGC | AACTGACCAG | CTCCAGGTTT | GATCAAACCA | 1920 |
| 40 | AAAGCAACAT | TTGTCATGTG | GTCTGACCAT | GTGGAGATGT | TTCTGGACTT | GCTAGAGCCT | 1980 |
| | GCTTAGCTGC | ATGTTTTGTA | GTTACGATTT | TTGGAATCCC | ACTTIGAGTG | CTGAAAGTGT | 2040 |
| 45 | AAGGAAGCTT | TCTTCTTACA | CCTTGGGCTT | GGATATTGCC | CAGAGAAGAA | ATTTGGCTTT | 2100 |
| 73 | TTTTTTNCTT | AATGGACAAG | AGACAGTTGC | TGTTCTCATG | TTCCAAGTCT | GAGAGCAACA | 2160 |
| | GACCCTCATC | ATCTGTGCCT | GGAAGAGTTC | ACTGTCATTG | AGCAGCACAG | CCTGAGTGCT | 2220 |
| 50 | GGCCTCTGTC | AACCCTTATT | CCACTGCCTT | ATTTGACAAG | GGGTTACATG | CTGCTCACCT | 2280 |
| | TACTGCCCTG | GGATTAAATC | AGTTACAGGC | CAGAGTCTCC | TTGGAGGGCC | TGGAACTCTG | 2340 |
| 55 | AGTCCTCCTA | TGAACCTCTG | TAGCCTAAAT | GAAATTCTTA | AAATCACCGA | TGGAACCAAA | 2400 |
| J J | АААААААА | ААААААААА | ААААААААА | AAAAN | | | 2435 |

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| (2) | INFORMATION | FOR | SEQ | ID | NO: | 108: |
|-----|-------------|-----|-----|----|-----|------|
|-----|-------------|-----|-----|----|-----|------|

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 805 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:

10 ATGAAACTTA AGAATTGAAT TGGAAAGACT TCTCAAAGAG AATTGTATGT AACGATGTTG 60 TATTGATTTT TAAGAAAGTA ATTTAATTTG TAAAACTTCT GCTCGTTTAC ACTGCACATT 120 15 GAATACAGGT AACTAATTGG AAGGAGAGGG GAGGTCACTC TTTTGATGGT GGCCCTGAAC 180 CTCATTCTGG TTCCCTGCTG CGCTGCTTGG TGTGACCCAC GGAGGATCCA CTCCCAGGAT 240 GACGTGCTCC GTAGCTCTGC TGCTGATACT GGGTCTGCGA TGCAGCGGCG TGAGGCCTGG 300 20 GCTGGTTGGA GAAGGTCACA ACCCTTCTCT GTTGGTCTGC CTTCTGCTGA AAGACTCGAG 360 AACCAACCAG GGAAGCTGTC CTGGAGGTCC CTGGTCGGAG AGGGACATAG AATCTGTGAC 420 25 CTCTGACAAC TGTGAAGCCA CCCTGGGCTA CAGAAACCAC AGTCTTCCCA GCAATTATTA 480 CAATTCTTGA ATTCCTTGGG GATTTTTTAC TGCCCTTTCA AAGCACTTAA GTGTTAGATC 540 TAACGTGTTC CAGTGTCTGT CTGAGGTGAC TTAAAAAATC AGAACAAAAC TTCTATTATC 600 30 CAGAGTCATG GGAGAGTACA CCCTTTCCAG GAATAATGTT TTGGGAAACA CTGAAATGAA ATCTTCCCAG TATTATAAAT TGTGTATTTA AAAAAAGAA ACTTTTCTGA ATGCCTACTG 720 35 GCGGTGTATA CCAGGCAGTG TGCCAGTTTA AAAAGATGAA AAAGAATAAA AACTTTTGAG 780 GAACAAAAA AAAAAAAAAA AAATT 805

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(2) INFORMATION FOR SEQ ID NO: 109:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1166 base pairs

(B) TYPE: nucleic acid (C) STRANDEDNESS: double

(D) TOPOLOGY: linear

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

GGCACGAGAG GCGCCAGTCG CAGGTGTGCT GCTGAGGCGT GAGAATGGCG TCCCGCGGCC 60 GGCGTCCGGA GCATGGCGGA CCCCCAGAGC TGTTTTATGA CGAGACAGAA GCCCGGAAAT 120 ACGTTCGCAA CTCACGGATG ATTGATATCC AGACCAGGAT GGCTGGGCGA GCATTGGAGC 180 TTCTTTATCT GCCAGAGAAT AAGCCCTGTT ACCTGCTGGA TATTGGCTGT GGCACTGGGC TGAGTGGAAG TTATCTGTCA GATGAAGGGC ACTATTGGGT GGGCCTGGAT ATCAGCCCTG 300

| | CCATGCTGGA | TGAGGCTGTG | GACCGAGAGA | TAGAGGGAGA | CCTGCTGCTG | GGGGATATGG | 360 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | GCCAGGGCAT | CCCATTCAAG | CCAGGCACAT | TTGATGGTTG | CATCAGCATT | TCTGCTGTGC | 420 |
| 3 | AGTGGCTCTG | TAATGCTAAC | AAGAAGTCTG | AAAACCCTGC | CAAGCGCCTG | TACTGCTTTT | 480 |
| | TIGCTTCTCT | TTTTTCTGTT | CTCGTCCGGG | GATCCCGAGC | TGTCCTGCAG | CTGTACCCTG | 540 |
| 10 | AGAACTCAGA | GCAGTTGGAG | CTGATCACAA | CCCAGGCCAC | AAAGGCAGGC | TTCTCCGGTG | 600 |
| | GCATGGTGGT | AGACTACCCT | AACAGTGCCA | AAGCAAAGAA | ATTCTACCTC | TGCTTGTTTT | 660 |
| 15 | CTGGGCCTTC | GACCTTTATA | CCAGAGGGGC | TGAGTGAAAA | TCAGGATGAA | GTTGAACCCA | 720 |
| 13 | GGGAGTCTGT | GTTCACCAAT | GAGAGGTTCC | CATTAAGGAT | GTCGAGGCGG | GGAATGGTGA | 780 |
| | GGAAGAGTCG | GGCATGGGTG | CTGGAGAAGA | AGGAGCGGCA | CAGGCGCCAG | GGCAGGGAAG | 840 |
| 20 | TCAGACCTGA | CACCCAGTAC | ACCGGCCGCA | AGCGCAAGCC | CCGCTTCTAA | GTCACCACGC | 900 |
| | GGTTCTGGAA | AGGCACTTGC | CTCTGCACTT | TTCTATATTG | TTCAGCTGAC | AAAGTAGTAT | 960 |
| 25 | TTTAGAAAAG | TTCTAAAGTT | ATAAAAATGT | TTTCTGCAGT | AAAAAAAAAG | TTCTCTGGGC | 1020 |
| 23 | CGGGCGTGGT | GGCTCACANC | TGTAATCCCA | GCACCTTGGG | AGGCTGAGGT | GGGAGGATCA | 1080 |
| | TTIGAGGCCA | GGAGTTTGAG | ACCTGCCTGG | GCAACATAAT | GAAACTTCCT | TTCCAGGGAG | 1140 |
| 30 | ААААААААА | AAAAAAAA | ACTCGA | | | | 1166 |

35 (2) INFORMATION FOR SEQ ID NO: 110:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 586 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

45 60 AGAGCGGACG AAGCTGGATA ACAGGGGACC GATGATGTGG CGACCATCAG TTCTGCTGCT TCTGTTGCTA CTGAGGCACG GGGCCCAGGG GAAGCCATCC CCAGACGCAG GCCCTCATGG 120 CCAGGGGAGG GTGCACCAGG CGGCCCCCCT GAGCGACGCT CCCCATGATG ACGCCCACGG 180 50 240 GAACTTCCAG TACGACCATG AGGCTTTCCT GGGACGGGAA GTGGCCAAGG AATTCGACCA ACTCACCCCA GAGGAAAGCC AGGCCCGTCT GGGGCGGATC GTGGACCGCA TGGACCGCGC 300 GGGGGACGCC GACGGCTGGG TGTCGCTGGC CGAGCTTCGC GCGTGGATCG CGCACACGCA 55 360 GCAGCGGCAC ATACGGGACT CGGTGAGCGC GGCCTGGGAC ACGTACGACA CGGACCGCGA 420 480 CGGGCGTGTG GGTTGGGAGG AGCTGCGCAA CGYCACCTAT GGCCACTASG SGCCCGKTGA 60

WO 98/42738 PCT/US98/05311

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| | AGAATTTCAT | GACGTGGAGG | ATGCAGAGAC | YTACAAAAAG | ATGCTGGYTC | GGGACGAGCG | 540 |
|----|-------------|--------------|---------------------------|-------------|------------|------------|------|
| | GCGTTTCCGG | GTGGCCGACC | AGGATGGGGA | CTCGATGGCC | ACTCGA | | 586 |
| 5 | | | | | | | |
| | (2) INFORMA | ATION FOR SE | EQ ID NO: 13 | 11: | | | |
| 10 | (i) | SEQUENCE CH | HARACTERIST | ICS: | | | |
| • | ,-, | (A) LEN | GTH: 1134 b E: nucleic | ase pairs | | | |
| | | (C) STR | ANDEDNESS: | double | | | |
| 15 | | (D) TOP | OLOGY: line | ar | | | |
| | (xi) |) SEQUENCE I | DESCRIPTION | : SEQ ID NO | : 111: | | |
| | ACCCATTGAG | CAGAAGGAGG | CCAGGTGGGA | AAGCTCCTGG | GAAGAGCAGC | CAGACTGGAC | 60 |
| 20 | ACTGGGCTGC | TTGAGTCCTG | AGTCACAATT | CAGAATTCCT | GGGCTCCCTG | GGTGCATTCT | 120 |
| | ATCATTCCAG | TTGAAAGTTT | GCTTCCTTCC | AGTCATGTGG | CTCTTCATTC | TACTCTCCTT | 180 |
| 25 | GGCTCTCATT | TCAGATGCCA | TGGTCATGGA | TGAAAAGGTC | AAGAGAAGTT | TGTGCTGGAC | 240 |
| 25 | ACGGCTTCTG | CCATCTGCAA | CTACAATGCC | CAYTACAAGA | ATCACCCCAA | ATACTGGTGC | 300 |
| | CGAGGYTATT | TCCGTGAYTA | CTGCAACATC | ATCGCCTTCT | CCCCTAACAG | CACCAATCAT | 360 |
| 30 | GTGGCCCTGA | AGGACACAGG | GAACCAGCTC | ATTGTCACTA | TGTCCTGCCT | GAACAAANAA | 420 |
| | GACACGGGCT | GGTACTGGTG | TGGCATCCAR | CGGGACTTTG | CMAGGGATGA | CATGGATTTT | 480 |
| 25 | ACAGAGCTGA | TTGTAACTGA | CGACAAAGGA | ACCCTGGCCA | ATGACTTTTG | GTCTGGGAAA | 540 |
| 35 | GACCTATCAG | GCAACAAAAC | CAGAAGCTGC | AAGGCTCCCA | AAGTTGTCCG | CAAGCTGACC | 600 |
| | GCTCCAGGAC | GTCCATTCTC | ATCATTTGCA | TACTGATCAC | GGGTTTGGGA | ATCATCTCTG | 660 |
| 40 | TAATCAGTCA | TTTGACCAAA | AGGAGGAGAA | GTCAAAGGAA | TAGAAGGGTA | GGCAACACTT | 720 |
| | TGAAGCCCTT | CTCGCGTGTC | CTGACTCCAA | AGGAAATGGC | TCCTACTGAA | CAGATGTGAC | 780 |
| | TGAAGWITTT | TTTAATTTAG | TTNCATAAAG | TGATGNCTAC | AACAGAWTAA | TCACCCATGA | 840 |
| 45 | CAACTGGCCC | CACACCTCAG | AGACTGATTC | TGATCTCCCA | GGAATTCTGA | AGGACCCTCT | 900 |
| | ATCCTTGACA | ACAATCATTT | GCAGCCAGGT | AGCAACGGCR | GTAGTCAGAG | GAGCTATGAT | 960 |
| 50 | AGACCACACC | CAAGCAAGGC | TGCCCTCAAA | TAACATCTCA | AGATCTTAGT | TCTTATGCAT | 1020 |
| | TCCATCAGTC | AGAAGTGAAG | AAGAGGTGGA | GAATCTKGAT | TGGGGACCAG | GAAATCACTT | 1080 |
| | GTATTTTGTT | AGCCAATAAA | TTCCTAGCCA | GTGTTGAATG | AAAAAAAA | AAAA | 1134 |
| 55 | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 112:

| | (i |) SEOUENCE | CHARACTERISTICS | 3: |
|--|----|------------|-----------------|----|
|--|----|------------|-----------------|----|

(A) LENGTH: 1333 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

| 10 | CACTTTAAAG | CTCTGCTGAG | GGAGTTCGGA | GCCCAGGCTT | TCAGGCGACC | TCTGCCCTCC | 60 |
|---------|------------|------------|------------|--------------|------------|------------|------|
| 10 | CTGCCTCTCC | TCACCCTCCC | TCTCTTCCTG | CAGGGCCTGG | GAAGGGCTTT | GAGGGAGCCT | 120 |
| | GGGAGCCATG | TGAAGAGGGG | CACGCCTGGG | CTGTCCCACA | GTTTAGATCC | AGTTGGAGGT | 180 |
| 15 | TCTCCCTGGC | TCCTGCAGGC | CTGCGGGGAT | CTCTCCCCAC | TTCAGGCCTC | CGGCAGCTGC | 240 |
| | CTGCCCTCTT | GTCTGTGCTT | CAGCCCTGCA | CAAAAGCAGC | TTGGTGACAC | CACTCAGCCA | 300 |
| 20 | CCCAGAGTAC | GTGTTTACAG | GCTTTCCAGA | TCACCTTCCT | GTGGGGTGAA | CGTAATGAGG | 360 |
| 20 | CGGGGCTGGT | CCTTGGAATT | TCCCCTGGAA | AATGGTAACA | GACTCCATCC | TTGACCCGGG | 420 |
| | GATGAGCATG | AAGGCATTGT | CCCAAAGGCA | GAGGCCACCG | TGGTAGGAAT | TCCACCAAGG | 480 |
| 25 | CCAGAAGGGA | AAAAGGAAGA | ACCCACCGTG | TCTGGCTGTG | CGGGCCCTGG | GGAGGGTCGT | 540 |
| | GAGTGCAGCC | CCTCTCTACT | TCYGTGCCTT | TGTAAAACGT | GTAGATAACC | GCAGTGGTTG | 600 |
| • | GCTGAGCCAA | GAACTCTCCT | AAATCAGTGG | CTTTCTCCCC | ACCCCTTGCT | GGGGAGTCAT | 660 |
| 30 | TTTTAAAAAA | ATCTGTGGGA | TATAAAATTG | GCCTCCTGCT | GCTTCAGCCT | ACCTCTCCCT | 720 |
| | CTGCTGACTT | AATGTCGTGA | TTCTGTTTCT | TCAGATATTT | AAGGCTGTTA | GGTTGTGTGA | 780 |
| 35 | GCCTTGAAGT | GTGTGTGTGT | GTCCCAGCGA | CTGTCCACTG | TCCAGGAGAT | GCATGTCTTT | 840 |
| | GTATTGGAGA | TATTTCTGTA | ACTCATTCTC | TTGGTGCTCA | CGATTGCCAT | GGCCATAGGG | 900 |
| 4.0 | CCACAGTGCC | GTATCTGCTG | CAGACATGAT | TGTTTCTTGT | TCTAGAGGTT | TTCTTGTTTT | 960 |
| 40 | CGAATCTTGC | CTGATGAATC | CAGCCAGACC | AAGGGCCTA | GATTTGACCT | CTGTCCTGGG | 1020 |
| | CTCCTGGGCC | AGGTGCAGGA | ACATCTGAGG | CCACTCTGCT | GGCCACCTCC | AGTGGGTGCT | 1080 |
| 45 | GACCACAGGA | TGGGCTTTGT | TTACACTCAT | TTTCACCCTG | ATTCTTGCCC | CCACTITCAT | 1140 |
| | AAAAGAAACT | TCAAAATGCT | GACGCTTTGG | G AGAGTAAGAA | AATCAATCTI | GGCTGGGCAC | 1200 |
| | GGTGGCTCCT | GCCTGTGATC | CTAGCACTT | GGGAGGCTGA | AGCTGAAGGA | TCACTTGAGC | 1260 |
| 50 | TCAGGAGTTG | GAGACCAACC | CTGGCAACAT | AACAAGACCC | TGTCTCTACA | AAAAAAAA | 1320 |
| | дадалаласт | CGA | | | | | 1333 |
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(2) INFORMATION FOR SEQ ID NO: 113:

60 (i) SEQUENCE CHARACTERISTICS:

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| (A) | LENGTH: 1015 base pairs |
|-----|-------------------------|
| (B) | TYPE: nucleic acid |
| (C) | STRANDEDNESS: double |
| (D) | TOPOLOGY: linear |

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113: GGCACGAGCG GCACGAGCGG CACGAGGTGA CTTCAAGTGT CGGATCTTTT CAGCCTACAT 60 10 CAAGGAGGTG GAGGAACGGC CGGCACCCAC CCCGTGGGCT CCAAGATGCC CTTTGGGGAA 120 CTGATGTTCG AATCCAGCAG TAGCTGCGGC TGGGTACATG GCGTCTGTTT CTCAGCCAGC 180 GGGAGCCGCG TGGCCTGGGT AAGCCACGAC AGCACCGTCT GCCTGGCTGA TGCCGACAAG 240 15 AAGATGCCCG TCGCGACTCT GGCCTCTGAA ACACTACCAC TGCTGGCGCT GACCTTCATC 300 ACAGACAACA GCCTGGTGGC AGCGGGCCAC GACTGCTTCC CGGTGCTGTT CACCTATGAC 360 20 GCCGCCGCGG GGATGCTGAG CTTCGGCGGG CGGCTGGACG TTCCTAAGCA GAGCTCGCAG 420 CGTGGCTTGA CGGCCCGCGA GCGCTTCCAG AACCTGGACA AGAAGGCGAG CTCCGAGGGT 480 GGCACGGCTG CGGCGCGGG CCTAGACTCG CTGCACAAGA ACAGCGTCAG CCAGATCTCG 540 25 GTGCTCAGCG GCGGCAAGGC CAAGTGCTCG CAGTTCTGCA CCACTGGCAT GGATGGCGGC 600 ATGAGTATCT GGGATGTGAA GAGCTTGGAG TCAGCCTTGA AGGACCTCAA GATCAAATGA 660 30 CCTGTGAGGA ATATGTTGCC TTCATCCTAG CTGCTGGGGA AGCGGGGAGA GGGGTCAGGG 720 AGGCTAATGG TTGCTTTGCT GAATGTTTCT GGGGTACCAA TACGAGTTCC CATAGGGGCT 780 GCTCCCTCAA AAAGGGAGGG GACAGATGGG GAGCTTTTCT TACCTATTCA AGGAATACGT 840 35 GCCTTTTCT TAAATGCTTT CATTTATTGA AAAAAAAAA AAATGCCCCC AAAGCACTAT 900 960

- 45 (2) INFORMATION FOR SEQ ID NO: 114:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1076 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

55 GGCACGAGGG GAAAGCCATG CTCCCAGGAC TCCTTCCTTG CAGCCTTAAA TCGGTCTGTA 60
CGGAAAATTC CGCGCCTTAG AAACCCACGC TTGGGTGTAA CTTATTATTG TTCTTCCTGA 120
CCTACTTCCT GTTTATCACT TCCGGGTTCA TCATTTTGGC ATTTCGGTGA TCGGGTTGGA 180

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| | ACTATTGAAG | CCCGCTTTCA | GGTTCTTTTC | CCCATTTTCC | CTTTGAAAGG | AAGACTTCTG | 240 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GCTTCTCCTA | AATCTCCGTT | CTCTGGGTAA | GGGGAGTCCA | AGCCTCTGTC | ATGAGGAACG | 300 |
| 5 | GAAATGCGAG | GCCTCGGGT | GTTACTCTAA | AATCCGCCCT | CAGCTTGCAC | GCCGGAAGCT | 360 |
| | GCGATTCCTG | CAGCGGAAGA | GGCGTGATCT | GGCCTTCGAC | TCGCTATGTC | CACTAACAAT | 420 |
| 10 | ATGTCGGACC | CACGGAGGCC | GAACAAAGTG | CTGAGGTACA | AGCCCCCGCC | GAGCGAATGT | 480 |
| 10 | AACCCGGCCT | TGGACGACCC | GACGCCGGAC | TACATGAACC | TGCTGGGCAT | GATCTTCAGC | 540 |
| | ATGTGCGGCC | TCATGCTTAA | GCTGAAGTGG | TGTGCTTGGG | TCGCTGTCTA | CTGCTCCTTC | 600 |
| 15 | ATCAGCTTTG | CCAACTCTCG | GAGCTCGGAG | GACACGAAGC | AAATGATGAG | TAGCTTCATG | 660 |
| | CTGTCCATCT | CTGCCGTGGT | GATGTCCTAT | CTGCAGAATC | CTCAGCCCAT | GACGCCCCCA | 720 |
| 20 | TGGTGATACC | AGCCTAGAAG | GGTCACATTT | TGGACCCTGT | CTATCCACTA | GGCCTGGGCT | 780 |
| 20 | TTGGCTGCTA | AACCTGCTGC | CTTCAGCTGC | CATCCTGGAC | TTCCCTGAAT | GAGGCCGTCT | 840 |
| | CGGTGCCCCC | AGCTGGATAG | AGGGAACCTG | GCCCTTTCCT | AGGGAACACC | CTAGGCTTAC | 900 |
| 25 | CCCTCCTGCC | TCCCTTCCCC | TGCCTGCTGC | TGGGGGAGAT | GCTGTCCATG | TTTCTAGGGG | 960 |
| | TATTCATTTG | CTTTCTCGTT | GAAACCTGTT | GTTAATAAAG | TTTTTCACTC | TGAAAAAAA | 1020 |
| 30 | AAAAAAANA | RAAAACNCGN | eeeeeeccc | GGAACCCAAT | TCSCCGGATA | GTGAGT | 1076 |
| | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 115:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1487 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

40 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

CCGCTGCTGA TAACTATGGC ATCCCCCGGG CCTGCAGGAA TTCGGCACGG AGCTACGGCG 60 45 CCGCCTGGCT CCTGCTGNCA CCTGCAGGCT CGTCGCGGGT GGAGCCCACC CAAGACATCA 120 GCATCAGCGA CCAGCTGGGG GGCCAGGACG TGCCCGTGTT CCGGAACCTG TCCCTGCTGG 180 240 50 TEGTEGETET CEGCECCETE TTCTCACTEC TATTCCACCT GEGCACCCGG GAGAGGCGCC 300 GGCCGCATGC GGASGAGCCA GGCGAGCACA CCCCCCTGTT GGCCCCTGCC ACGGCCCAGC CCCTGCTGCT CTGGAAGCAC TGGCTCCGGG AGCSGGCTTT CTACCAGGTG GGCATACTGT 360 55 ACATGACCAC CAGGCTCATC GTGAACCTGT CCCAGACCTA CATGGCCATG TACCTCACCT 420 ACTCGCTCCA CCTGCCCAAG AAGTTCATCG CGACCATTCC CCTGGTGATG TACCTCAGCG 480 540 GCTTCTTGTC CTCCTTCCTC ATGAAGCCCA TCAACAAGTG CATTGGGAGG AACATGACCT 60

| | ACTTCTCAGG | CCTCCTGGTG | ATCCTGGCCT | TTGCCGCCTG | GGTGGCGCTG | GCGGAGGGAC | 600 |
|----|------------|------------|------------|------------|------------|------------|---------------|
| 5 | TGGGTGTGGC | CGTGTACGCA | GCGGCTGTGC | TGCTGGGTGC | TGGCTGTGCC | ACCATCCTCG | 660 |
| 5 | TCACCTCGCT | GGCCATGACG | GCCGACCTCA | TCGGTCCCCA | CACGAACAGC | GGAGCKTTCG | 720 |
| | TGTACGGCTC | CATGAGCTTC | TTGGATAAGG | TGGCCAATGG | GCTGGCAGTC | ATGGCCATCC | 780 |
| 10 | AGAGCCTGCA | CCCTTGCCCC | TCAGAGCTCT | GCTGCAGGGC | CTGCGTGAGC | TTTTACCACT | 840 |
| | GGGCGATGGT | GGCTGTGACG | GGCGGCGTGG | GCGTGGCCGC | TGCCCTGTGT | CTCTGTAGCC | 900 |
| 15 | TCCTGCTGTG | GCCGACCCGC | CTGCGACGCT | GATGAGACCT | GCACGCANTG | GCTCACAGCA | 960 |
| 13 | GCACGATTTG | TGACAGCCCG | AGGCGGAGAA | CACCGAACAC | CCAGTGAAGG | TGAGGGGATC | 1020 |
| | AGCACGGCGC | GGCCACCCAC | GCACCCACGC | GCTGGAATGA | GACTCAGCCA | CAAGGAGGTG | 1080 |
| 20 | CGAAGCTCTG | ACCCAGGCCA | CAGTGCGGAT | GCACCTTGAG | GATGTCACGC | TCAGTGAGAG | 1140 |
| | ACACCAGACA | CAGAAGGGTA | CGCTGTGATC | CCACTTCTAT | GAAATGTCCA | GGACAGACCA | 1200 |
| 25 | ATCCACAGAA | TCAGGGAGAG | GATTCGTGGG | TGCCGGGACT | GGGGAGGGG | ACCTGGGGGT | 1260 |
| 23 | GACTAGGTGA | CATAATGGGG | ACAGGGCTGC | CTTCTGGGTG | ATGAGAATGT | TCTGGAATCA | 1320 |
| | GATGGGATGG | CTGCACGGCG | TGGTGAAGGT | ACTGAACGCC | ACCTCACTGT | AAGACGGTAG | 1380 |
| 30 | ATTTTGTATT | TTACCACAAT | AAACAAAACA | AAACAAAACC | АААААААА | AAAAAAAA | 1440 |
| | AAAAAAAAGG | AATTCGATAT | CAAGCTTATC | GATACCGTCG | ACCTCGA | | 1 4 87 |
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(2) INFORMATION FOR SEQ ID NO: 116:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1350 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

GGCACGAGTG CGCANGCGTG GGGCTCTCTC CTTGTCAGTC GGCGCCGCGT GCGGGCTGGT 60 GGCTCTGTGG CAGCGCGGC GGCAGGACTC CGGCACTATG AGCGGCTTCA GCACCGAGGA 120 50 GCGCGCGCG CCTTCTCCCT GGAGTACCGA GTCTTCCTCA AAAATGAGAA AGGACAATAT 180 ATATCTCCAT TYCATGATAT TCCAATTTAT GCAGATAAGG ATGTGTTTCA CATGGTAGTT 240 55 GAAGTACCAC GCTGGTCTAA TGCAAAAATG GAGATTGCTA CAAAGGACCC TTTAAACCCT 300 ATTAAACAAG ATGTGAAAAA AGGAAAACTT CGCTATGTTG CGAATTTGTT CCCGTATAAA 360 GGATATATCT GGAACTATGG TGCCATCCCT CAGACTTGGG AAGACCCAGG GCACAATGAT 420 60

| | AAACATACTG | GCTGTTGTGG | TGACAATGAC | CCAATTGATG | TGTGTGAAAT | TGGAAGCAAG | 480 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GTATGTGCAA | GAGGTGAAAT | AATTGGCGTG | AAAGTTCTAG | GCATATTGGC | TATGATTGAC | 540 |
| 5 | GAAGGGGAAA | CCGACTGGAA | AGTCATTGCC | ATTAATGTGG | ATGATCCTGA | TGCAGCCAAT | 600 |
| | TATAATGATA | TCAATGATGT | CAAACGGCTG | AAACCTGGCT | ACTTAGAAGC | TACTGTGGAC | 660 |
| 10 | TGGTTTAGAA | GGTATAAGGT | TCCTGATGGA | AAACCAGAAA | ATGAGTTTGC | GTTTAATGCA | 720 |
| 10 | GAATTTAAAG | ATAAGGACTT | TGCCATTGAT | ATTATTAAAA | GCACTCATGA | CCATTGGAAA | 780 |
| | GCATTAGTGA | CTAAGAAAAC | GAATGGAAAA | GGAATCAGTT | GCATGAATAC | AACTTTGTCT | 840 |
| 15 | GAGAGCCCCT | TCAAGTGTGA | TCCTGATGCT | GCCAGAGCCA | TTGTGGATGC | TTTACCACCA | 900 |
| | CCCTGTGAAT | CTGCCTGCAC | AGTACCAACA | GACGTGGATA | AGTGGTTCCA | TCACCAGAAA | 960 |
| 20 | AACTAATGAG | ATTTCTCTGG | AATACAAGCT | GATATTGCTA | CATCGTGTTC | ATCTGGATGT | 1020 |
| 20 | ATTAGAAGTA | AAAGTAGTAG | CTTTTCAAAG | CTTTAAATTT | GTAGAACTCA | TCTAACTAAA | 1080 |
| | GTAAATTCTG | CTGTGACTAA | TCCAATATAC | TCAGAATGTT | ATCCATCTAA | AGCATTTTTC | 1140 |
| 25 | ATATCTCAAC | TAAGATAACT | TTTAGCACAT | GCTTAAATAT | CAAAGCAGTT | GTCATTTGGA | 1200 |
| | AGTCACTTGT | GAATAGATGT | GCAAGGGGAG | CACATATTGG | ATGTATATGT | TACCATATGT | 1260 |
| 20 | TAGGAAATAA | AATTATTTTG | CTGAAAAAA | АААААААА | ACCTSGGGG | GGGSCCCGGT | 1320 |
| 30 | CCCCATTIGG | CCCTTTGGGG | GGNGGTTTTA | | | | 1350 |

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(2) INFORMATION FOR SEQ ID NO: 117:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2527 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

45 CTCTTGCTAC CTTCCCGGCG CAGAGAACCC CGGCTGCTCA GCGCGCTCCG GGGTCATGGA 60 GATCCCCGGG AGCCTGTGCA AGAAAGTCAA GCTGAGCAAT AACGCGCAGA ACTGGGGAAT 120 50 GCAGAGAGCA ACCAATGTCA CCTACCAAGC CCATCATGTC AGCAGGAACA AGAGAGGTCA 180 GGTGGTGGGG ACCAGAGGTG GCTTTCGTGG TTGCACAGTT TGGCTAACAG GCTTGTCTGG 240 AGCGGGAAAG ACTACTGTGA GCATGGCCTT GGAGGAGTAC CTGGTTTGTC ATGGTATTCC 300 55 ATGCTACACT CTGGATGGTG ACAATATTCG TCAAGGTCTC AATAAAAATC TTGGCTTTAG 360 TCCTGAAGAC AGAGAAGAGA ATGTTCGACG CATCGCAGAA GTTGCTAAAC TGTTTGCAGA 420 60 480 TGCTGGCTTA GTGTGCATCA CAAGTTTCAT ATCACCTTAC ACTCAGGATC GCAACAATGC

| | AAGGCAAA'1"1' | CATGAAGGTG | CAAGTTTACC | GTTTTTGAA | GIATITGITG | ATGCTCCTCT | 540 |
|-----|---------------|------------|------------|------------|------------|------------|------|
| 5 | GCATGTTTGT | GAACAGAGGG | ATGTCAAAGG | ACTCTACAAA | AAAGCCCGGG | CAGGAGAAAT | 600 |
| 5 | TAAAGGTTTC | ACTGGGATCG | ATTCTGAATA | TGAAAAGCCA | GAGGCCCCTG | AGTTGGTGCT | 660 |
| | GAAAACAGAC | TCCTGTGATG | TAAATGACTG | TGTCCAGCAA | GTTGTGGAAC | TTCTACAGGA | 720 |
| 10 | ACGGGATATT | GTACCTGTGG | ATGCATCTTA | TGAAGTAAAA | GAACTATATG | TGCCAGAAAA | 780 |
| | TAAACTTCAT | TTGGCAAAAA | CAGATGCGGA | AACATTACCA | GCACTGAAAA | TTAATAAAGT | 840 |
| 1 = | GGATATGCAG | TGGGTGCAGG | TTTTGGCAGA | AGGTTGGGCA | ACCCCATTGA | ATGGCTTTAT | 900 |
| 15 | GAGAGAGAGG | GAGTACTTGC | AGTGCCTTCA | TTTTGATTGT | CTTCTGGATG | GAGGTGTCAT | 960 |
| | TAACTTGTCA | GTACCTATAG | TTCTGACTGC | GACTCATGAA | GATAAAGAGA | GGCTGGACGG | 1020 |
| 20 | CTGTACAGCA | TTTGCTCTGA | TGTATGAGGG | CCGCCGTGTG | GCCATTCTTC | GCAATCCAGA | 1080 |
| | GTTTTTTGAG | CACAGGAAAG | AGGAGCGCTG | TGCCAGACAG | TGGGGAACGA | CATGCAAGAA | 1140 |
| 25 | CCACCCCTAT | ATTAAGATGG | TGATGGAACA | AGGAGATTGG | CTGATTGGAG | GAGATCTTCA | 1200 |
| 23 | AGTCTTGGAT | CGAGTTTATT | GGAATGATGG | TCTTGATCAG | TATCGTCTTA | CTCCTACTGA | 1260 |
| | GCTAAAGCAG | AAATTTAAAG | ATATGAATGC | TGATGCTGTC | TTTGCATTTC | AACTACGCAA | 1320 |
| 30 | CCCAGTGCAC | AATGGACATG | CCCTGTTAAT | GCAGGATACC | CATAAGCAAC | TTCTAGAGAG | 1380 |
| | GGGCTACCGG | CGCCCTGTCC | TCCTCCTCCA | CCCTCTGGGT | GGCTGGACAA | AGGATGACGA | 1440 |
| 35 | TGTTCCTTTG | ATGTGGCGTA | TGAAGCAGCA | TGCTGCAGTG | TTGGAGGAAG | GAGTTCTGAA | 1500 |
| 55 | TCCTGAGACG | ACAGTGGTGG | CCATCTTCCC | ATCTCCCATG | ATGTATGCTG | GACCAACTGA | 1560 |
| | GGTCCAGTGG | CATTGCAGAG | CACGGATGGT | TGCAGGAGCC | AACTTTTACA | TTGTTGGACG | 1620 |
| 40 | AGACCCTGCT | GGCATGCCTC | ATCCAGAAAC | AGGGAAGGAT | CTTTATGAGC | CAAGTCATGG | 1680 |
| | TGCCAAAGTG | CTGACGATGG | CCCCTGGTTT | AATCACTTTG | GAAATAGTTC | CCTTTCGAGT | 1740 |
| 45 | TGCAGCTTAC | AACAAGAAAA | AGAAGCGTAT | GGACTACTAT | GACTCTGAAC | ACCATGAAGA | 1800 |
| | CTTTGAATTT | ATTICAGGAA | CACGAATGCG | CAAACTTGCT | CGAGAAGGCC | AGAAACCACC | 1860 |
| | TGAAGGTTTC | ATGGCTCCCA | AGGCTTGGAC | CGTGCTGACA | GAATACTACA | AATCCTTGGA | 1920 |
| 50 | GAAAGCTTAG | GCTGTTAACC | CAGTCACTCC | ACCTTTGACA | CATTACTAGT | AACAAGAGGG | 1980 |
| | GACCACATAG | TCTCTGTTGG | CATTTCTTTG | TGGTGTCTGT | CTGGACATGC | TTCCTAAAAA | 2040 |
| 55 | CAGACCATTT | TCCTTAACTT | GCATCAGTTT | TGGTCTGCCT | TATGAGTTCT | GTTTTGAACA | 2100 |
| | AGTGTAACAC | ACTGATGGTT | TTAATGTATC | TTTTCCACTT | ATTATAGTTA | TATTCCTACA | 2160 |
| | ATACAATTTT | AAAATTGTCT | ATTATATTTT | TATTTATGCT | TCTGTGTCAT | GATTTTTTCA | 2220 |
| 60 | AGCTGTTATA | TTAGTTGTAA | CCAGTAGTAT | TCACATTAAA | TCTTGCTTTT | TTTCCCCTTA | 228 |

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| 10 | АААААА | | | | | | 2527 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GTAAGCTCTG | AATGAACTTC | TTTACTCAAT | AAAATTAATT | TTTTGGCTTC | TTAAAAAAA | 2520 |
| 5 | CTTTCCAGTC | AGCTATTGGT | CTTTCCAGCT | GTTATAATCT | AAAGTATTCT | TATGATCTGT | 2460 |
| | AGACCTTTGT | AGCGATTAGA | TTTTTTTCT | ACATTGAAAA | TAGAAACTGC | TTCCTTTCTT | 2400 |
| | AAAAAGAAA | AAAATTACCA | AACAATAAAC | TTGGCTAGAC | CTTGTTTTGA | GGATTTTACA | 2340 |

15 (2) INFORMATION FOR SEQ ID NO: 118:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1098 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

| 25 | CGCATCACAG | ACAACCCAGA | AGGAAAATGG | TTGGGCAGAA | CAGCAAGGGG | TTCATATGGC | 60 |
|----|------------|------------|------------|-------------|------------|------------|------|
| | TATATTAAAA | CAACTGCTGT | AGAGATTNNC | TATGATTCTT | TGAAACTGAA | AAAAGACTCT | 120 |
| 30 | CTTGGTGCCC | CTTCAAGACC | TATTGAAGAT | GACCAAGAAG | TATATGATGA | TGTTGCAGAG | 180 |
| 30 | CAGGATGATA | TTAGCAGCCA | CAGTCAGAGT | GGAAGTGGAG | GGATATTCCC | TCCACCACCA | 240 |
| | GATGATGACA | TTTATGATGG | GATTGAAGAG | GAAGATGCTG | ATGATGGTTT | CCCTGCTCCT | 300 |
| 35 | CCTAAACAAT | TGGACATGGG | AGATGAAGTT | TACGATGATG | TGGATACCTC | TGATTTCCCT | 360 |
| | GTTTCATCAG | CAGAGATGAG | TCAAGGAACT | AATGTTGGAA | AAGCTAAGAC | AGAAGAAAAG | 420 |
| 40 | GACCTTAAGA | AGCTAAAAA | GCAGRAAAA | GAARAAAAAG | ACTTCAGGAA | AAATTTAAA | 480 |
| 40 | TATGATGGTG | AAATTAGAGT | CCTATATTCA | ACTAAAGTTA | CAACTTCCAT | AACTTCTAAA | 540 |
| | AAGTGGGGAA | CCAGAGATCT | ACAGGTAAAA | CCTGGTGAAT | CTCTAGAAGT | TATACAAACC | 600 |
| 45 | ACAGATGACA | CAAAAGTTCT | CTGCAGAAAT | GAAGAAGGGA | AATATGGTTA | TGTCCTTCGG | 660 |
| | AGTTACCTAG | CGGACAATGA | TGGAGAGATC | TATGATGATA | TTGCTGATGG | CTGCATCTAT | 720 |
| 50 | GACAATGACT | AGCACTCAAC | TTTGGTCATT | CTGCTGTGTT | CATTAGGTGC | CAATGTGAAG | 780 |
| 50 | TCTGGATTTT | AATTGGCATG | TTATTGGGTA | TCMAGAAAAT | TAATGCACAR | AACCACTTAT | 840 |
| | TATCATTTGT | TATGAAATCC | CAATTATCTT | TACAAAGTGT | TTAAAGTTTG | AACATAGAAA | 900 |
| 55 | ATAATCTCTC | TGCTTAATTG | TTATCTCAGA | AGACTACATT | AGTGAGATGT | AAGAATTATT | 960 |
| | AAATATTCCA | TTTCCGCTTT | GGCTACAATT | ATGAAGAAGT | TGAAGGTACT | TCTTTTAGAC | 1020 |
| 60 | CACCAGTAAA | TAATCCTCCT | ТСАААААТА | . ААААТАААА | AAAAAAAA | AAACTCGAGG | 1080 |

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| GGGGG | SCCCGG TACCCAAT | 1098 |
|-------|-----------------|------|
| | | |
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(2) INFORMATION FOR SEQ ID NO: 119:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1679 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

15 TCGACCCACG CGTCCGGCGA GATCCCTACC GCAGTAGCCG CCTCTGCCGC CGCGGAGCTT 60 CCCGAACCTC TTCAGCCGCC CGGAGCCGCT CCCGGAGCCC GGCCGTAGAG GCTGCAATCG 120 20 CAGCCGGGAG CCCGCAGCCC GCGCCCCGAG CCCGCCGCCG CCCTTCGAGG GCGCCCCAGG 180 CCGCGCCATG GTGAAGGTGA CGTTCAACTC CGCTCTGGCC CAGAAGGAGG CCAAGAAGGA 240 CGAGCCCAAG AGCGCGAGG AGGCGCTCAT CATCCCCCC GACGCCGTCG CGGTGGACTG 300 25 CAAGGACCCA GATGATGTGG TACCAGTTGG CCAAAGAAGA GCCTGGTGTT GGTGCATGTG 360 CTTTGGACTA GCATTTATGC TTGCAGGTGT TATTCTAGGA GGAGCATACT TGTACAAATA 420 30 TTTTGCACTT CAACCAGATG ACGTGTACTA CTGTGGAATA AAGTACATCA AAGATGATGT 480 CATCTTAAAT GAGCCCTCTG CAGATGCCCC AGCTGCTCTC TACCAGACAA TTGAAGAAAA 540 TATTAAAATC TTTGAAGAAG AAGAAGTTGA ATTTATCAGT GTGCCTGTCC CAGAGTTTGC 600 35 AGATAGTGAT CCTGCCAACA TTGTTCATGA CTTTAACAAG AAACTTACAG CCTATTTAGA 660 TCTTAACCTG GATAAGTGCT ATGTGATCCC TCTGAACACT TCCATTGTTA TGCCACCCAG 720 40 AAACCTACTG GAGTTACTTA TTAACATCAA GGCTGGAACC TATTTGCCTC AGTCCTATCT 780 GATTCATGAG CACATGGTTA TTACTGATCG CATTGAAAAC ATTGATCACC TGGGTTTCTT 840 TATTTATCGA CTGTGTCATG ACAAGGAAAC TTACAAACTG CAACGCAGAG AAACTATTAA 900 45 AGGTATTCAG AAACGTGAAG CCAGCAATTG TTTCGCAATT CGGCATTTTG AAAACAAATT 960 TGCCGTGGAA ACTTTAATTT GTTCTTGAAC AGTCAAGAAA AACATTATTG AGGAAAATTA 1020 50 ATATCACAGC ATAACCCCAC CCTTTACATT TTGTGCAGTG ATTATTTTTT AAAGTCTTCT 1080 TTCATGTAAG TAGCAAACAG GGCTTTACTA TCTTTTCATC TCATTAATTC AATTAAAACC 1140 ATTACCTTAA AATTTTTTC TTTCGAAGTG TGGTGTCTTT TATATTTGAA TTAGTAACTG 1200 55 TATGAAGTCA TAGATAATAG TACATGTCAC CITAGGTAGT AGGAAGAATT ACAATTTCTT 1260 TAAATCATTT ATCTGGATTT TTATGTTTTA TTAGCATTTT CAAGAAGACG GATTATCTAG 1320 60 AGAATAATCA TATATATGCA TACGTAAAAA TGGACCACAG TGACTTATTT GTAGTTGTTA 1380

| | GTTGCCCTGC | TACCTAGTTT | GTTAGTGCAT | TTGAGCACAC | ATTTTAATTT | TCCTCTAATT | 1440 |
|----|---------------------|------------|------------|------------|------------|------------|------|
| 5 | AAAATGTGCA | GTATTTTCAG | TGTCAAATAT | ATTTAACTAT | TTAGAGAATG | ATTTCCACCT | 1500 |
| 3 | TTATGTTTTA | ATATCCTAGG | CATCTGCTGT | AATAATATT | TAGAAAATGT | TTGGAATTTA | 1560 |
| | AGAAATAACT | TGTGTTACTA | ATTTGTATAA | CCCATATCTG | TGCAATGGAA | TATAAATATC | 1620 |
| 10 | ACAAAGT T GT | TTAAMWAAAA | АААААААА | ААААААААА | AAAAAAAA | NAAAAAAA | 1679 |
| | | | | | | | |

15 (2) INFORMATION FOR SEQ ID NO: 120:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1308 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

| 25 | TTGGCANCNG | GGAGAGGGAA | AGAGGAGGAA | ATGGGGTTTG | AGGACCATGG | CTTACCTTTC | 60 |
|----|------------|------------|------------|------------|------------|------------|-------------|
| | CTGCCTTTGA | CCCATCACAC | CCCATTTCCT | CCTCTTTCCC | TCTCCCCGCT | GCCAAAAAAA | 120 |
| 30 | AAAAAAAAGG | AAACGTTTAT | CATGAATCAA | CAGGGTTTCA | GTCCTTATCA | AAGAGAGATG | 180 |
| 50 | TGGAAAGAGC | TAAAGAAACC | ACCCTTTGTT | CCCAACTCCA | CTTTACCCAT | ATTTTATGCA | 240 |
| | ACACAAACAC | TGTCCTTTTG | GGTCCCTTTC | TTACAGATGG | ACCTCTTGAG | AAGAATTATC | 300 |
| 35 | GTATTCCACG | TTTTTAGCCC | TCAGGTTACC | AAGATAAATA | TATGTATATA | TAACCTTTAT | 360 |
| | TATTGCTATA | TCTTTGTGGA | TAATACATTC | AGGTGGTGCT | GGGTGATTTA | TTATAATCTG | 4 20 |
| 40 | AACCTAGGTA | TATCCTTTGG | TCTTCCACAG | TCATGTTGAG | GTGGGCTCCC | TGGTATGGTA | 4 80 |
| 10 | AAAAGCCAGG | TATAATGTAA | CTTCACCCCA | GCCTTTGTAC | TAAGCTCTTG | ATAGTGGATA | 540 |
| | TACTCTTTTA | AGTTTAGCCC | CAATATAGGG | TAATGGAAAT | TTCCTGCCCT | CTGGGTTCCC | 600 |
| 45 | CATTTTTACT | ATTAAGAAGA | CCAGTGATAA | TTTAATAATG | CCACCAACTC | TGGCTTAGTT | 660 |
| | AAGTGAGAGT | GTGAACTGTG | TGGCAAGAGA | GCCTCACACC | TCACTAGGTG | CAGAGAGCCC | 7 20 |
| 50 | AGGCCTTATG | TTAAAATCAT | GCACTTGAAA | AGCAAACCTT | AATCTGCAAA | GACAGCAGCA | 780 |
| 20 | AGCATTATAC | GGTCATCTTG | AATGATCCCT | TTGAAATTTT | TTTTTTTTTT | GTTTGTTTAA | 840 |
| | ATCAAGCCTG | AGGCTGGTGA | ACAGTAGCTA | CACACCCATA | TTGTGTGTTC | TGTGAATGCT | 900 |
| 55 | AGCTCTCTTG | AATTTGGATA | TTGGTTATTT | TTTATAGAGT | GTAAACCAAG | TTTTATATTC | 960 |
| | TGCAATGCGA | ACAGGTACCT | ATCTGTTTCT | AAATAAAACT | GTTTACATTC | ATTATGGGGT | 1020 |
| 60 | ATGTATGACC | TTCATTTTCC | AAGAAATAGA | ACTCTAGCTT | AGAATTATGG | ATGCTCTAAA | 1080 |

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PCT/US98/05311

1080

1140

1200

ATGTCAGAAT GGGAACTCTC CTCGAAGTTC TCCCAAACTC AGAGACAGCA CTGCCTTCTC 1140 CTAAATGATT ATTCTTTTCT CCCTGTTTTC TGGTATTTTC TAGGCATCCT TCTCACCACA 1200 5 GCCATAACCC TTTTTTACTT CCATTAGGCC GTATAACTGG NGGGACNGCT GGTCGGTATA 1260 TAATACTGGT WCCAACAMAG GGGTTCTGGA TGTACACMAG GTTATCTT 1308 10 (2) INFORMATION FOR SEQ ID NO: 121: (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 1411 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121: GCCACAGGAG CGACCCGGGA GAAGGAGGGC CAMGAKGCGG AAGCGGAGGA GTCTCCAGGA 60 GACCGGGGA CAGCATCGCC CAGGCCCCTG TTTGCAGGCC TTTCAGATAT ATCCATCTCA 120 25 CAAGACATCC CCGTAGAAGG AGAAATCACC ATTCCTATGA GATCTCGCAT CCGGGAGTTT 180 GACAGCTCCA CATTAAATGA ATCTGTTCGC AATACCATCA TGCGTGATCT AAAAGCTGTT 240 30 GGGAAAAAT TCATGCATGT TTTGTACCCA AGGAAAAGTA ATACTCTTTT GAGAGATTGG 300 GATTIGTGGG GCCCTTTGAT CCTTTGTGT ACACTCGCAT TAATGCTGCA AAGAGACTCT 360 GCAGATAGTG AAAAAGATGG AGGGCCCCAA TTTGCAGAGG TGTTTGTCAT TGTCTGGTTT 420 35 GGTGCAGTTA CCATCACCCT CAACTCAAAA CTTCTTGGAG GGAACATATC TTTTTTCAG 480 AGCCTCTGTG TGCTGGGTTA CTGTATACTT CCCTTGACAG TAGCAATGCT GATTTGCCGG 540 40 CTGGTACTTT TGGCTGATCC AGGACCTGTA AACTTCATGG TTCGGCTTTT TGTGGTGATT 600 GTGATGTTTG CCTGGTCTAT AGTTGCCTCC ACAGCTTTCC TTGCTGATAG CCAGCCTCCA 660 AACCGCAGAG CCCTAGCTGT TTATCCTGTT TTCCTGTTTT ACTTTGTCAT CAGTTGGATG 720 45 ATTCTCACCT TTACTCCTCA GTAAATCAGG AATGGGAAAT TAAAAACCAG TGAATTGAAA 780 GCACATCTGA AAGATGCAAT TCACCATGGA GCTTTGTCTC TGGCCCTTAT TTGTCTAATT 840 50 TTGGAGGTAT TTGATAACTG AGTAGGTGAG GAGATTAAAA GGGAGCCATA TAGCACTGTC 900 ACCCCTTATT TGAGGAACTG ATGTTTGAAA GGCTGTTCTT TTCTCTCTTA ATGTCATTTC 960 TTTAAAAATA CATGTGCATA CTACACACAG TATATAATGC CTCCTTAAGG CATGATGGAG 1020 55

TCACCGTGGT CCATTTGGGT GACAACCAGT GACTTGGGAA GCACATAGAT ACATCTTACA

AGTTGAATAG AGTTGATAAC TATTTTCAGT TTTGAGAATA CCAGTTCAGG TGCAGCTCTT

AAACACATTG CCTTATGACT ATTAGAATAT GCCTCTCTTT TCATAAATAA AAATACATGG

| | TCTATATCCA TTTTCTTTTA TTTCTCTCTC TTAAGCTTAA AAAGGCAATG AGAGAGGTTA | 1260 |
|----|---|------|
| 5 | GGAGTGGGTT CATACACGGA GAATGAGAAA ACATGCATTA ACCAATATTC AGATTTTGAT | 1320 |
| 3 | CAGGGGAAAT TCTAYACTTG TTGCAAAAAA AAAAAAAAA AAACTCGAGG GGGCCCGGT | 1380 |
| | ACCCAATCGC NGTATATGAT CGNAAACAAT C | 1411 |
| 10 | | |
| | (2) INFORMATION FOR SEQ ID NO: 122: | |
| 15 | (i) SEQUENCE CHARACTERISTICS: | |
| 10 | (A) LENGTH: 2256 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double | |
| 20 | (D) TOPOLOGY: linear | |
| 20 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122: | |
| | GCTTTGGCTT TTTTTGGCGG ACTGGGGCGC CCTCCGGAAG CGTTTCCAAC TTTCCAGAAG | 60 |
| 25 | TTTCTCGGGA CGGGCAGGAG GGGGTGGGGA CTGCCATATA TAGATCCCGG GAGCAGGGGA | 120 |
| | GCGGGCTAAG AGTAGAATCG TGTCGCGGCT CGAGAGCGAG AGTCACGTCC CGGCGCTAGC | 180 |
| 30 | CAGCCCGACC CAGGCCCACC GTGGTGCACG CAAACCACTT CCTGGCCATG CGCTCCCTCC | 240 |
| 50 | TGCTTCTCAG CGCCTTCTGC CTCCTGGAGG CGGCCCTGGC CGCCGAGGTG AAGAAACCTG | 300 |
| | CAGCCGCAGC AGCTCCTGGC ACTGCGGAGA AGTTGAGCCC CAAGGCGGCC ACGCTTGCCG | 360 |
| 35 | AGCGCANGCC GGCCTGGCCT TCAGCTTGTA CCAGGCCATG GCCAAGGACC AGGCAGTGGA | 420 |
| | GAACATCCTG GTGTCACCCG TGGTGGTGGC CTCGTCGCTG GGGCTCGTGT CGCTGGGCGG | 480 |
| 40 | CAAGGCGACC ACGGCGTCGC AGGCCAAGGC AGTGCTGAGC GCCGAGCAGC TGCGCGACGA | 540 |
| 70 | GGAGGTGCAC GCCGGCCTGG GCGAGCTGCT GCGCTCACTC AGCAACTCGA CGGCGCGCAA | 600 |
| | CGTGACCTGG AAGCTGGGCA GCCGACTGTA CGGACCCAGC TCAGTGAGCT TCGCTGATGA | 660 |
| 45 | CTTCGTGCGC ACAGCAAGCA GCACTACAAC TGCGAGCACT CCAAGATCAA CTTCCGCGAC | 720 |
| | AAGCGCAGNG CGCTGCAGTC CATCAACGAG TGGGCCGCGC AGACCACCGA CGGCAAGCTG | 780 |
| 50 | CCCGAGGTCA CCAAGGACGT GGAGCGCACG GACGGCGCCC TGCTAGTCAA CGCCATGTTC | 840 |
| 50 | TTCAAGCCAC ACTGGGATGA GAAATTCCAC CACAAGATGG TGGACAACCG TGGCTTCATG | 900 |
| | GTGACTCGGT CCTATACYGT GGGTGTCATG ATGATGCACC GGACAGGCCT CTACAACTAC | 960 |
| 55 | TACGACGACG AGAAGGAAAA GCTGCAAATC GTGGAGATGC CCCTGGCCCA CAAGCTCTCC | 1020 |
| | AGCCTCATCA TCCTCATGCC CCATCACGTG GAGCCTCTCG AGCGCCTTGA AAAGCTGCTA | 1080 |
| 60 | ACCAAAGAGC AGCTGAAGAT CTGGATGGGG AAGATGCAGA AGAAGGCTGT TGCCATCTCC | 1140 |
| | | |

| | TTGCCCAAGG | GTGTGGTGGA | GGTGACCCAT | GACCTGCAGA | AACACCTGGC | TGGGCTGGGC | 1200 |
|----|-------------|--------------|-----------------------------|-------------|------------|------------|------|
| | CTGACTGAGG | CCATTGACAA | GAACAAGGCC | GACTTRTCAC | GCATGTCAGG | CAAGAAGGAC | 1260 |
| 5 | CTGTACCTGG | CCAGCGTGTT | CCACGCCACC | GCCTTTGAGT | TGGACACAGA | TGGCAACCCC | 1320 |
| | TTTGACCAGG | ACATCTACGG | GCGCGAGGAG | CTGCGCANCC | CAAGCTGTTC | TACGCCGACC | 1380 |
| 10 | ACCCCTTCAT | CTTCCTAGTG | CGGGACACCC | AAAGCGGCTC | CCTGCTATTC | ATTGGGCGCC | 1440 |
| 10 | TGGTCCGGCC | TAAGGGTGAC | AAGATGCGAG | ACGAGTTATA | GGGCCTCAGG | GTGCACACAG | 1500 |
| | GATGGCAGGA | GGCATCCAAA | GGCTCCTGAG | ACACATGGGT | GCTATTGGGG | TTGGGGGGGA | 1560 |
| 15 | GGTGAGGTAC | CAGCCTTGGA | TACTCCATGG | GGTGGGGGTG | GAAAARCAGA | CCGGGGTTCC | 1620 |
| | CGTGTGCCTG | AGCGGACCTT | CCCAGCTAGA | ATTCACTCCA | CTTGGACATG | GGCCCCAGAT | 1680 |
| 20 | ACCATGATGC | TGAGCCCGGA | AACTCCACAT | CCTGTGGGAC | CTGGGCCATA | GTCATTCTGC | 1740 |
| 20 | CTGCCCTGAA | AGTCCCAGAT | CAAGCCTGCC | TCAATCAGTA | TTCATATTTA | TAGCCAGGTA | 1800 |
| | CCTTCTCACC | TGTGAGACCA | AATTGAGCTA | GGGGGGTCAG | CCAGCCCTCT | TCTGACACTA | 1860 |
| 25 | AAACACCTCA | GCTGCCTCCC | CAGCTCTATC | CCAACCTCTC | CCAACTATAA | AACTAGGTGC | 1920 |
| | TGCAGCCCCT | GGGACCAGGC | ACCCCCAGAA | TGACCTGGCC | GCAGTGAGGC | GGATTGAGAA | 1980 |
| 30 | GGAGCTCCCA- | GGAGGGGCTT | CTGGGCAGAC | TCTGGTCAAG | AAGCATCGTG | TCTGGCGTTG | 2040 |
| 50 | TGGGGATGAA | CTTTTTGTTT | TGTTTCTTCC | TTTTTTAGTT | CTTCAAAGAT | AGGGAGGGAA | 2100 |
| | GGGGAACAT | GAGCCTTTGT | TGCTATCAAT | CCAAGAACTT | ATTTGTACAT | TTTTTTTTC | 2160 |
| 35 | AATAAAACTT | TTCCAATGAC | АААААААА | АААААААА | AAAAAGGGGS | GGGCCGCTCC | 2220 |
| | TAGAGGGATC | CCTCCGANGG | NGCCCAATCG | AAAATN | | | 2256 |
| 40 | | | | | | | |
| 10 | (2) INFORMA | ATTON FOR SE | EQ ID NO: 12 |)3. | | | |
| | | | | | | | |
| 45 | (i) | | HARACTERIST: GTH: 829 ba | | | | |
| | | • • | E: nucleic | | | | |
| | | | ANDEDNESS: OLOGY: line | | | | |
| 50 | (xi |) SEQUENCE 1 | DESCRIPTION | : SEQ ID NO | : 123: | | |
| | ATGCGCTCCC | TCCTGCTTCT | CAGCGCCTTC | TGCCTCCTGG | AGGCGGCCCT | GGCCGCCGAG | 60 |
| | GTGAAGAAAC | CTGCAGCCGC | AGCAGCTCCT | GGCACTGCGG | AGAAGTTGAG | CCCCAAGGCG | 120 |
| 55 | GCCACGCTTG | CCGAGCGCAA | GCGGCCTGGC | CTTCAGCTTG | TACCAGGCCA | TGGCCAAGGA | 180 |
| | CCAGGCAGTG | GAGAACATCC | TGGTGTCACC | CGTGGTGGTG | GCCTCGTCGC | TGGGGCTCGT | 240 |
| | | | | | | | |

GTCGCTGGGC GGCAAGGCGA CCACGGCGTC GCAGGCCAAG GCAGTGCTGA GCGCCGAGCA

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| | GCTGCGCGAC | GAGGAGGTGC | ACGCCGGCCT | GGGCGAGCTG | CTGCGCTCAC | TCAGCAACTC | 360 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 5 | CACGGCGCGC | AACGTGACCT | GGAAGCTGGG | CAGCCGACTG | TACGGACCCA | GCTCAGTGAG | 420 |
| ڔ | CTTCGCTGAT | GACTTCGTGC | GCAGCAGCAA | GCAGCACTAC | AACTGCGAGC | ACTCCAAGAT | 480 |
| | CAACTTCCGC | GACAAGCGCA | GCGCGCTGCA | GTCCATCAAC | GAGTGGGCCG | CGCAGACCAC | 540 |
| 10 | CGACGGCAAG | CTGCCCGAGG | TCACCAAGGA | CGTGGAGCGC | ACGGACGGCG | CCCTGTTAGT | 600 |
| | CAACGCCATG | TTCTTCAAGC | CACACTGGGA | TGAGAAATTC | CACCACAAGA | TGGTGGACAA | 660 |
| 15 | CCGTGGCTTC | ATGGTGACTC | GGTCCTATAC | CGTGGGTGTC | ATGATGATGC | ACCGGACAGG | 720 |
| 10 | CCTCTACAAC | TACTACGACG | ACGAGAAGGA | AAAGCTGCAA | ATCGTGGAGA | TGCCCCTGGC | 780 |
| | CCACAAGCTC | TCCAGCCTCA | TCATCCTCAT | GCCCCATCAC | GTGGAGCCT | | 829 |

20

(2) INFORMATION FOR SEQ ID NO: 124:

25 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2223 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

| | CCTCCGGAAG | CGTTTCCAAC | TTTCCAGAAG | TTTCTCGGGA | CGGGCAGGAG | GGGGTGGGGA | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 35 | CTGCCATATA | TAGATCCCGG | GAGCAGGGGA | GCGGGCTAAG | AGTAGAATCG | TGTCGCGGCT | 120 |
| | CGAGAGCGAG | AGTCACGTCC | CGGCGCTAGC | CAGCCCGACC | CAGGCCCACC | GTGGTGCACG | 180 |
| 40 | CAAACCACTT | CCTGGCCATG | CGCTCCCTCC | TGCTTCTCAG | CGCCTTCTGC | CTCCTGGAGG | 240 |
| 40 | CGGCCCTGGC | CGCCGAGGTG | AAGAAACCTG | CAGCCGCAGC | AGCTCCTGGC | ACTGCGGAGA | 300 |
| | AGTTGAGCCC | CAAGGCGGCC | ACGCTTGCCG | AGCGCAGNCG | GCCTGGCCTT | CAGCTTGTAC | 360 |
| 45 | CAGGCCATGG | CCAAGGACCA | GGCAGTGGAG | AACATCCTGG | TGTCACCCGT | GGTGGTGGCC | 420 |
| | TCGTCGCTGG | GGCTCGTGTC | GCTGGGCGGC | AAGGCGACCA | CGGCGTCGCA | GGCCAAGGCA | 480 |
| 50 | GTGCTGAGCG | CCGAGCAGCT | GCGCGACGAG | GAGGTGCACG | CCGGCCTGGG | CGAGCTGCTG | 540 |
| 30 | CGCTCACTCA | GCAACTCSAC | GGCGCGCAAC | GTGACCTGGA | AGCTGGGCAG | CCGACTGTAC | 600 |
| | GGACCCAGCT | CAGTGAGCTT | CGCTGATGAC | TTCGTGCGCA | CAGCAAGCAG | CACTACAACT | 660 |
| 55 | GCGAGCACTC | CAAGATCAAC | TICCGCGACA | AGCGCACGCG | CTGCAGTCCA | TCAACGAGTG | 720 |
| | GGCCGCGCAG | ACCACCGACG | GCAAGCTGCC | CGAGGTCACC | AAGGACGTGG | AGCGCACGGA | 780 |
| 60 | CGGCGCCCTG | YTAGTCAACG | CCATGTTCTT | CAAGCCACAC | TGGGATGAGA | AATTCCACCA | 840 |

| | CAAGATGGTG | GACAACCGTG | GCTTCATGGT | GACTCGGTCC | TATACYGTGG | GTGTCATGAT | 900 |
|------------|------------|------------|------------|------------|------------|------------|------|
| | GATGCACCGG | ACAGGCCTCT | ACAACTACTA | CGACGACGAG | AAGGAAAAGC | TGCAAATCGT | 960 |
| 5 | GGAGATGCCC | CTGGCCCACA | AGCTCTCCAG | CCTCATCATC | CTCATGCCCC | ATCACGTGGA | 1020 |
| | GCCTCTCGAG | CGCCTTGAAA | AGCTGCTAAC | CAAAGAGCAG | CTGAAGATCT | GGATGGGGAA | 1080 |
| 10 | GATGCAGAAG | AAGGCTGTTG | CCATCTCCTT | GCCCAAGGGT | GTGGTGGAGG | TGACCCATGA | 1140 |
| 10 | CCTGCAGAAA | CACCTGGCTG | GGCTGGGCCT | GACTGAGGCC | ATTGACAAGA | ACAAGGCCGA | 1200 |
| | CTTRTCACGC | ATGTCAGGCA | AGAAGGACCT | GTACCTGGCC | AGCGTGTTCC | ACGCCACCGC | 1260 |
| 15 | CTTTGAGTTG | GACACAGATG | GCAACCCCTT | TGACCAGGAC | ATCTACGGGC | GCGAGGAGCT | 1320 |
| | GCGCASCCCA | AGCTGTTCTA | CGCCGACCAC | CCCTTCATCT | TCCTAGTGCG | GGACACCCAA | 1380 |
| 20 | AGCGGCTCCC | TGCTATTCAT | TGGGCGCCTG | GTCCGGCCTA | AGGGTGACAA | GATGCGAGAC | 1440 |
| 20 | GAGTTATAGG | GCCTCAGGGT | GCACACAGGA | TGGCAGGAGG | CATCCAAAGG | CTCCTGAGAC | 1500 |
| | ACATGGGTGC | TATTGGGGTT | GGGGGGAGG | TGAGGTACCA | GCCTTGGATA | CTCCATGGGG | 1560 |
| 25 | TGGGGTGGA | AAARCAGACC | GGGGTTCCCG | TGTGCCTGAG | CGGACCTTCC | CAGCTAGAAT | 1620 |
| | TCACTCCACT | TGGACATGGG | CCCCAGATAC | CATGATGCTG | AGCCCGGAAA | CTCCACATCC | 1680 |
| 30 | TGTGGGACCT | GGGCCATAGT | CATTCTGCCT | GCCCTGAAAG | TCCCAGATCA | AGCCTGCCTC | 1740 |
| 30 | AATCAGTATT | CATATTTATA | GCCAGGTACC | TTCTCACCTG | TGAGACCAAA | TTGAGCTAGG | 1800 |
| | GGGTCAGCC | AGCCCTCTTC | TGACACTAAA | ACACCTCAGC | TGCCTCCCCA | GCTCTATCCC | 1860 |
| 35 | AACCTCTCCC | AACTATAAAA | CTAGGTGCTG | CAGCCCCTGG | GACCAGGCAC | CCCCAGAATG | 1920 |
| | ACCTGGCCGC | AGTGAGGCGG | ATTGAGAAGG | AGCTCCCAGG | AGGGGCTTCT | GGGCAGACTC | 1980 |
| 40 | TGGTCAAGAA | GCATCGTGTC | TGGCGTTGTG | GGGATGAACT | TTTTGTTTTG | TTTCTTCCTT | 2040 |
| 4 0 | TTTTAGTTCT | TCAAAGATAG | GGAGGGAAGG | GGGAACATGA | GCCTTTGTTG | CTATCAATCC | 2100 |
| | AAGAACTTAT | TTGTACATTT | TTTTTTCAA | TAAAACTTTT | CCAATGACAA | ААААААААА | 2160 |
| 45 | AAAAAAAA | MWMGGGGSGG | GCCGCTCCTA | GAGGGATCCC | TCCGANGGNG | CCCAATCGAA | 2220 |
| | AAT | | | | | | 2223 |

55

(2) INFORMATION FOR SEQ ID NO: 125:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

60 Met Lys Lys Gln Ser Lys Arg Cys Leu Trp Lys Pro Pro Gly Ser Leu

| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
|----|----------|-----|------------------|----------------|-------------------------|-------------------------|----------------------|-----------------------------|----------------------|-----------|-----|---------------|------------|-----------|-----------|-----|
| 5 | Arg | Arg | Leu | Trp 20 | Trp | Met | Arg | Ala | Leu 25 | Leu | Ile | Leu | Lys | Туr 30 | Ile | |
| 10 | (2) | | ORMAC | | | | | | | : | | | | | | |
| 10 | | | (xi) | (; (; (; | A) L B) T D) T | ENGT: YPE: OPOL | H: 4 ami OGY: | 5 am no a lin | ino cid ear | acid | | : 12 | 6 : | | | |
| 15 | Met 1 | | Lys | _ | | | | | | | | | | Met | Leu 15 | Leu |
| 20 | | | Thr | 20 | | | | | 25 | | | | | Leu 30 | Thr | Thr |
| 25 | Arg | Mec | 35 | ьеч | GIÀ | rne | GIII | 40 | FIO | 1115 | Бей | 1111 | 45 | | | |
| | (2) | INF | ORMA! | | | | | NO: : | | | | | | | | |
| 30 | | | | (| A) L B) T D) T | ENGT YPE : 'OPOL | H: 3 ami OGY: | 9 am no a lin PTIO | ino cid ear | acid | | : 12 | 7: | | | |
| 35 | Met 1 | His | Asn | Gln | Arg 5 | Gln | Val | Phe | Leu | Phe 10 | His | Leu | Phe | Ser | Asn 15 | Tyr |
| 40 | | | Ser Asn 35 | 20 | | | | Pro | Gly 25 | Thr | Leu | Leu | Ala | Ala 30 | Thr | Tyr |
| 45 | (2) | INF | 'ORMA' | TION | FOR | SEQ | ID | NO: | 128: | | | | | | | |
| 50 | | | | ~ (| (A) I (B) T (D) T | ENGT TYPE : TOPOL | TH: 2 ami OGY: | ERIS an ino a ino in | mino ncid near | ació | |): 1 2 | 8 : | | | |
| 55 | Met 1 | | l Lys | Lys | Phe 5 | | Leu | Ala | Gln | Val | | Leu | Ser | Leu | Ser 15 | Val |
| | Met | Pro | Ser | Met 20 | | Val | Thr | | | | | | | | | |
| 60 | | | | | | | | | | | | | | | | |

| | (2) | INF | PAMAC | NOI | FOR | SEQ | ID N | 10: 1 | 29: | | | | | | | |
|-----|-----------|-----------|------------|----------------|-----------------------|-----------------------|-----------------------|---------------------------------|--------------------|-----------|-----------|-------------|-----------|------------|-----------|-----------|
| .5 | | | (i) s | (2 (1 (1 | A) Li B) T D) T | ENGT YPE : OPOL | H: 1: ami: OGY: | 10 ar no ao line | mino cid ear | acio | | : 129 | 9∶ | | | |
| 10 | Met 1 | Val | Leu | Leu | Cys 5 | Leu | Leu | Leu | Val | Pro 10 | Leu | Leu | Leu | Ser | Leu 15 | Phe |
| 1.5 | Val | Leu | Gly | Leu 20 | Phe | Leu | Trp | Phe | Leu 25 | Lys | Arg | Glu | Arg | Gln 30 | Glu | Glu |
| 15 | Tyr | Ile | Glu 35 | Glu | Lys | Lys | Arg | Val 40 | Asp | Ile | Cys | Arg | Glu 45 | Thr | Pro | Asn |
| 20 | Ile | Cys 50 | Pro | His | Ser | Gly | Glu 55 | Asn | Thr | Glu | Tyr | Asp 60 | Thr | Ile | Pro | His |
| | Thr 65 | | Arg | Thr | Ile | Leu 70 | Lys | Glu | Asp | Pro | Ala 75 | Asn | Thr | Val | Tyr | Ser 80 |
| 25 | Thr | Val | . Glu | Ile | Pro 85 | | Lys | Met | Glu | Asn 90 | Pro | His | Ser | Leu | Leu 95 | Thr |
| 30 | Met | Pro | Asp | Thr 100 | | Arg | Leu | Phe | Ala 105 | | Glu | Asn | Val | Ile 110 | | |
| | (2) | INE | FORMA | TION | FOR | SEQ | ID | NO: | 130: | | | | | | | |
| 35 | | | (i) | | (A) I (B) : | LENG: TYPE | rh: 6 : ami | ERIS 53 an ino a : lir | nino acid | | ds | | | | | |
| 40 | | | | SEÇ | QUENC | CE DE | ESCR] | PTIC | N: 5 | | | | | Dwo | T/ol | Dro |
| | : | 1 | u Lev | | Ē | 5 | | | | 10 |) | | | | 15 | |
| 45 | | | y Ala | 20 |) | | | | 25 | 5 | | | | 30 | | |
| | | | r Val | 5 | | | | 40 |) | | | | 45 | 5 | | |
| 50 | Le | | y Arg O | g Lei | ı Glı | u Gli | n Met | | e His | s Phe | e Gly | y Let 60 | | a Ser | Gly | , |
| 55 | (2 |) IN | FORM | ATIOI | N FO | R SE | Q ID | NO: | 131 | : | | | | | | |
| | | | (i) | SEQ | (A) | LENG | TH: | TERI: 30 a ino | mino | aci | .ds | | | | | |
| 60 | | | | | | | | : li | | | | | | | | |

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:
     Met Pro Phe Pro Ile Ser Ile Leu Gln Leu Cys Leu Gln Ile Ser Asn
 5
     Leu Ser Phe Cys Leu Gln Lys Ile Tyr Lys Ile Pro Phe Val
                                 25
10
      (2) INFORMATION FOR SEQ ID NO: 132:
             (i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 53 amino acids
15
                    (B) TYPE: amino acid
                    (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:
     Met Ala Ala Cys Arg Ser Val Lys Gly Leu Val Ala Val Ile Thr
20
     Gly Gly Ala Ser Gly Leu Gly Leu Ala Thr Ala Asp Asp Leu Trp Gly
                                     25
25
      Arg Glu Pro Leu Cys Phe Trp Thr Cys Pro Thr Arg Val Gly Arg
                                  40
      Pro Lys Pro Arg Ser
          50
30
      (2) INFORMATION FOR SEQ ID NO: 133:
35
             (i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 57 amino acids
                    (B) TYPE: amino acid
                    (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:
40
      Met Leu Leu Val Tyr Asp Leu Tyr Leu Xaa Pro Lys Leu Trp Ala Leu
      Ala Thr Pro Gln Lys Asn Gly Lys Gly Ala Arg Xaa Gly Asp Gly Thr
45
      Pro Ala Gln Ala Phe Trp Asp Phe Trp Ser His Leu Ile Ser Ala Asp
50
      Pro Gln Thr Trp Glu Arg Ala Ala Pro
55
      (2) INFORMATION FOR SEQ ID NO: 134:
             (i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 216 amino acids
                    (B) TYPE: amino acid
60
                    (D) TOPOLOGY: linear
```

| | | | (xi) | SEQ | UENCI | E DE | SCRI | PTIO | N: SI | EQ II | O NO | : 134 | 4: | | | |
|----|------------|------------|------------|------------|-------------------------|------------|------------|------------|------------|------------|------------|---------------|------------|------------|------------|------------|
| 5 | Met 1 | Arg | Leu | Ser | Ala 5 | Leu | Leu | Ala | Leu | Ala 10 | Ser | Lys | Val | Thr | Leu 15 | Pro |
| 3 | Pro | His | Tyr | Arg 20 | Tyr | Gly | Met | Ser | Pro 25 | Pro | Gly | Ser | Val | Ala 30 | Asp | Lys |
| 10 | Arg | Ĺys | Asn 35 | Pro | Pro | Trp | Ile | Arg 40 | Arg | Arg | Pro | Val | Val 45 | Val | Glu | Pro |
| | Ile | Ser 50 | Asp | Glu | Asp | Trp | Tyr 55 | Leu | Phe | Суз | Gly | Asp 60 | Thr | Val | Glu | Ile |
| 15 | Leu 65 | Glu | Gly | Lys | Asp | Ala 70 | Gly | Lys | Gln | Gly | Lys 75 | Val | Val | Gln | Val | Ile 80 |
| 20 | Arg | Gln | Arg | Asn | Trp 85 | Val | Val | Val | Gly | Gly 90 | Leu | Asn | Thr | His | Tyr 95 | Arg |
| | Tyr | Ile | Gly | Lys 100 | Thr | Met | Asp | Tyr | Arg 105 | Gly | Thr | Met | Ile | Pro 110 | Ser | Glu |
| 25 | Ala | Pro | Leu 115 | Leu | His | Arg | Gln | Val 120 | Lys | Leu | Val | Asp | Pro 125 | Met | Asp | Arg |
| | Lys | Pro 130 | Thr | Glu | Ile | Glu | Trp 135 | Arg | Phe | Thr | Glu | Ala 140 | Gly | Glu | Arg | Val |
| 30 | Arg 145 | Val | Ser | Thr | Arg | Ser 150 | Gly | Arg | Ile | Ile | Pro 155 | Lys | Pro | Glu | Phe | Pro 160 |
| 35 | Arg | Ala | Asp | Gly | 11e 165 | Val | Pro | Glu | Thr | Trp 170 | Ile | Asp | Gly | Pro | Lys 175 | Asp |
| | | | Val | 180 | | | | | 185 | | | | | 190 | | |
| 40 | Thr | Leu | Gln 195 | | Glu | Va1 | Met | Glu 200 | | Met | Gly | Ile | Lys 205 | Glu | Thr | Arg |
| | Lys | Туг 210 | Lys | Lys | Val | Tyr | Trp 215 | | | | | | | | | |
| 45 | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 135: | | | | | | | |
| 50 | | | (i) | | JENCE (A) I | | | | | | ds | | | | | |
| | | | (xi) | | (B) I (D) I QUENC | ropoi | LOGY: | lir | near | SEQ] | D NO |): 1 3 | 15: | | | |
| 55 | Met 1 | | Leu | . Arg | Gln 5 | | : Ser | Ser | Phe | e Arg | | Met | . Val | Met | Ser 15 | Leu |
| | Thr | : Ile | e Leu | Lys 20 | | Ser | : Lys | Thr | Thr 25 | | . Leu | Cys | : Leu | Arg | | Leu |
| 60 | | | | | | | | | | | | | | | | |

| | His | Ser | Leu 35 | Lys | Leu | Thr | Trp | Arg 40 | Asp | Gly | Ala | Arg | Cys 45 | Ile | Asn | Ala |
|----|-----------|-----------|------------|-------------------|----------------------|------------------------|---------------|----------------------|--------------------|-----------|------|-----------|------------|-----------|-----------|-----|
| 5 | Glu | | | | | | | | | | | | | | | |
| 10 | (2) | INF | ORMAT | SEQUI () () | ENCE A) L B) T | CHAI ENGT: YPE: | RACTI H: 6 | ERIS 8 am no a | rICS ino cid | | s | | | | | |
| 15 | | | (xi) | SEQ | | OPOL | | | | EQ II | ON C | : 136 | 5 : | | | |
| | Met 1 | Ser | Gly | Ser | Phe 5 | Ile | Leu | Cys | Leu | Ala 10 | Leu | Val | Thr | Arg | Trp 15 | Ser |
| 20 | Pro | Gln | Ala | Ser 20 | Ser | Val | Pro | Leu | Ala 25 | Val | Tyr | Glu | Ser | Lys 30 | Thr | Arg |
| 25 | Lys | Ser | Tyr 35 | Arg | Ser | Gln | Arg | Asp 40 | Arg | Asp | Gly | Lys | Asp 45 | Arg | Ser | Gln |
| 43 | Gly | Met 50 | Gly | Leu | Ser | Leu | Leu 55 | Val | Glu | Thr | Arg | Lys 60 | Leu | Leu | Leu | Ser |
| 30 | Ala 65 | Asn | Gln | Gly | | | | | | | | | | | | |
| 35 | (2) | INF | ORMA | SEQU)) | ENCE A) L B) T | | RACT H: 5 | ERIS 2 am no a | TICS ino cid | | ls | | | | | |
| 40 | | | (xi) | SEQ | | | | | | EQ I | D NO | : 13 | 7: | | | |
| | Met 1 | _ | : Phe | Arg | Phe 5 | Phe | Leu | Phe | Cys | Ser 10 | Arg | Ile | Leu | Leu | Lys 15 | Leu |
| 45 | Phe | Ph∈ | e Leu | Leu 20 | Phe | Pro | Ala | Ser | Ala 25 | | Pro | Leu | Ser | Thr 30 | Arg | Ser |
| 50 | Ser | Leu | ser 35 | | Asn | Gl u | His | Val 40 | | Val | Ser | Pro | Arg 45 | Ser | Thr | Val |
| | Ser | 11e | e Ser) | Arg | | | | | | | | | | | | |
| 55 | (2) | INI | FORMA | MOIT | FOR | SEQ | ID | NO: | 138: | | | | | | | |
| 60 | | | (i) | | (A) I | E CHA LENGT LYPE | rH: ! | 541 á | amino | | ids | | | | | |

(D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

| 5 | Met 1 | Val | Arg | Thr | Asp 5 | Gly | His | Thr | Leu | Ser 10 | Glu | Lys | Arg | Asn | Tyr 15 | Gln |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | Val | Thr | Asn | Ser 20 | Met | Phe | Gly | Ala | Ser 25 | Arg | Lys | Lys | Phe | Val 30 | Glu | Gly |
| 10 | Val | Asp | Ser 35 | Asp | Tyr | His | Asp | Glu 40 | Asn | Met | Tyr | Tyr | Ser 45 | Gln | Ser | Ser |
| 15 | Met | Phe 50 | Pro | His | Arg | Ser | G1u 55 | Lys | Asp | Met | Leu | Ala 60 | Ser | Pro | Ser | Thr |
| | Ser 65 | Gly | Gln | Leu | Ser | Gln 70 | Phe | Gly | Ala | Ser | Leu 75 | Tyr | Gly | Gln | Gln | Ser 80 |
| 20 | Ala | Leu | Gly | Leu | Pro 85 | Met | Arg | Gly | Met | Ser 90 | Asn | Asn | Thr | Pro | Gln 95 | Leu |
| | Asn | Arg | Ser | Leu 100 | Ser | Gln | Gly | Thr | Gln 105 | Leu | Pro | Ser | His | Val 110 | Thr | Pro |
| 25 | Thr | Thr | Gly 115 | Val | Pro | Thr | Met | Ser 120 | Leu | His | Thr | Pro | Pro 125 | Ser | Pro | Ser |
| 30 | Arg | Gly 130 | Ile | Leu | Pro | Met | Asn 135 | Pro | Xaa | Asn | Met | Met 140 | Asn | His | Ser | Gln |
| | Val 145 | Gly | Gln | Gly | Ile | Gly 150 | Ile | Pro | Ser | Arg | Thr 155 | Asn | Ser | Met | Ser | Ser 160 |
| 35 | Ser | Gly | Leu | Gly | Ser 165 | Pro | Asn | Arg | Ser | Ser 170 | Pro | Ser | Ile | Ile | Cys 175 | Met |
| | Pro | Lys | Gln | Gln 180 | Pro | Ser | Arg | Gln | Pro 185 | Phe | Thr | Val | Asn | Ser 190 | Met | Ser |
| 40 | Gly | Phe | Gly 195 | Met | Asn | Arg | Asn | Gln 200 | Ala | Phe | Gly | Met | Asn 205 | Asn | Ser | Leu |
| 45 | Ser | Ser 210 | Asn | Ile | Phe | Asn | Gly 215 | Thr | Asp | Gly | Ser | Glu 220 | Asn | Val | Thr | Gly |
| 15 | Leu 225 | Asp | Leu | Ser | | Phe 230 | | Ala | Leu | | Asp 235 | Arg | Asn | Arg | Arg | Glu 240 |
| 50 | Gly | Ser | Gly | Asn | Pro 245 | Thr | Pro | Leu | Ile | Asn 250 | Pro | Leu | Ala | Gly | Arg 255 | Ala |
| | Pro | Туг | Val | Gly 260 | Met | Val | Thr | Lys | Pro 265 | Ala | Asn | Glu | Gln | Ser 270 | Gln | Asp |
| 55 | Phe | Ser | Ile 275 | His | Asn | Glu | Asp | Phe 280 | Pro | Ala | Leu | Pro | Gly 285 | Ser | Ser | Тут |
| 60 | Lys | Asp 290 | Pro | Thr | Ser | Ser | Asn 295 | Asp | Asp | Ser | Lys | Ser 300 | Asn | Leu | Asn | Thr |

| | Ser 305 | Gly | Lys | Thr | Thr | Ser 310 | Ser | Thr | Asp | Gly | Pro 315 | Lys | Phe | Pro | Gly | Asp 320 |
|----|------------|------------|------------|------------|--------------|--------------|-------------|-----------------------|---------------|------------|--------------------|------------|------------|------------|------------|------------|
| 5 | Lys | Ser | Ser | Thr | Thr 325 | Gln | Asn | Asn | Asn | Gln 330 | Gln | Lys | Lys | Gly | Ile 335 | Gln |
| | Val | Leu | Pro | Asp 340 | Gly | Arg | Val | Thr | Asn 345 | Ile | Pro | Gln | Gly | Met 350 | Val | Thr |
| 10 | Asp | Gln | Phe 355 | Gly | Met | Ile | Gly | Leu 360 | Leu | Thr | Phe | Ile | Arg 365 | Ala | Ala | Glu |
| 15 | Thr | Asp 370 | Pro | Gly | Met | Val | His 375 | Leu | Ala | Leu | Gly | Ser 380 | Asp | Leu | Thr | Thr |
| 13 | Leu 385 | Gly | Leu | Asn | Leu | Asn 390 | Ser | Pro | Glu | Asn | Leu 395 | Tyr | Pro | Lys | Phe | Ala 400 |
| 20 | Ser | Pro | Trp | Ala | Ser 405 | Ser | Pro | Cys | Arg | Pro 410 | Gln | Asp | Ile | Asp | Phe 415 | His |
| | Val | Pro | Ser | Glu 420 | Tyr | Leu | Thr | Asn | Ile 425 | His | Ile | Arg | Asp | Lys 430 | Leu | Ala |
| 25 | Ala | Ile | Lys 435 | Leu | Gly | Arg | Tyr | Gly 440 | Glu | Asp | Leu | Leu | Phe 445 | Tyr | Leu | Tyr |
| 30 | Tyr | Met 450 | Asn | Gly | Gly | Asp | Val 455 | Leu | Gln | Leu | Leu | Ala 460 | Ala | Val | Glu | Leu |
| 30 | Phe 465 | Asn | Arg | Asp | Trp | Arg 470 | Туг | His | Lys | Glu | Glu 47 5 | Arg | Val | Trp | Ile | Thr 480 |
| 35 | Arg | Ala | Pro | G1y | Met 485 | Glu | Pro | Thr | Met | Lys 490 | Thr | Asn | Thr | Tyr | Glu 495 | Arg |
| | Gly | Thr | Tyr | Tyr 500 | Phe | Phe | Asp | Cys | Leu 505 | Asn | Trp | Arg | Lys | Val 510 | Ala | Lys |
| 40 | Glu | Phe | His 515 | Leu | Glu | Tyr | Asp | Lys 520 | Leu | Glu | Glu | Arg | Pro 525 | His | Leu | Pro |
| 45 | Ser | Thr 530 | Phe | Asn | Tyr | Asn | Pro 535 | Ala | Gln | Gln | Ala | Phe 540 | Xaa | | | |
| | (2) | INFO | ORMAT | rion | FOR | SEQ | ID 1 | 1 0: 1 | L 3 9: | | | | | | | |
| 50 | | | (i) : | (| A) L B) T | ENGT YPE: | H: 5 ami | ERIS' 8 am no a | ino d | | s | | | | | |
| 55 | | | (xi) | | | | | lin PTIO | | EQ II | D NO | : 13 | 9: | | | |
| | Met 1 | Ile | Cys | Pro | Gln 5 | Cys | Pro | Leu | Ser | Leu 10 | Leu | Cys | Leu | Ile | Ser 15 | Ser |
| 60 | Leu | Cys | Ser | Leu 20 | Val | Ile | Gln | Ile | Ser 25 | Leu | Lys | Thr | Ile | Arg 30 | Asp | Ile |

| | Thr | Leu | Leu 35 | Asn | Met | Val | Gly | Ile 40 | Lys | Phe | Ser | Ile | Ser 45 | Leu | Ser | Asn |
|-----|------------|------------|---------------|---------------|----------------------|-----------------------|----------------------|---------------------|--------------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Lys | Ile 50 | Asn | Ile | Asn | Ser | Arg 55 | Thr | Trp | Xaa | | | | | | |
| 10 | (2) | INF | ORMAT | rion | FOR | SEQ | ID 1 | NO: 1 | 140: | | | | | | | |
| 15 | | | (i) : (xi) | - (: (: | A) L B) T D) T | ENGT YPE : OPOL | H: 2 ami: OGY: | 02 a no a lin | mino cid ear | aci | | : 14 | 0: | | | |
| 20 | Met 1 | Thr | Leu | Arg | Pro 5 | Ser | Leu | Leu | Pro | Leu 10 | His | Leu | Leu | Leu | Leu 15 | Leu |
| 20 | Leu | Leu | Ser | Ala 20 | Ala | Val | Cys | Arg | Ala 25 | Glu | Ala | Gly | Leu | Glu 30 | Thr | Glu |
| 25 | Ser | Pro | Val 35 | Arg | Thr | Leu | Gln | Val 40 | Glu | Thr | Leu | Val | Glu 45 | Pro | Pro | Glu |
| | Pro | Cys 50 | Ala | Glu | Pro | Ala | Ala 55 | Phe | Gly | Asp | Thr | Leu 60 | His | Ile | His | Туг |
| 30 | Thr 65 | Gly | Ser | Leu | Val | Asp 70 | Gly | Arg | Ile | Ile | Asp 75 | Thr | Ser | Leu | Thr | Arg 80 |
| 2.5 | Asp | Pro | Leu | Val | Ile 85 | Glu | Leu | Gly | Gln | Lys 90 | Gln | Val | Ile | Pro | Gly 95 | Leu |
| 35 | Glu | Gln | Ser | Leu 100 | Leu | Asp | Met | Cys | Val 105 | Gly | Glu | Lys | Arg | Arg 110 | Ala | Ile |
| 40 | Ile | Pro | Ser 115 | His | Leu | Ala | Tyr | Gly 120 | Lys | Arg | Gly | Phe | Pro 125 | Pro | Ser | Val |
| | Pro | Ala 130 | Asp | Ala | Val | Val | Gln 135 | Tyr | Asp | Val | Glu | Leu 140 | Ile | Ala | Leu | Ile |
| 45 | Arg 145 | | Asn | Tyr | Trp | Leu 150 | Lys | Leu | Val | Lys | Gly 155 | Ile | Leu | Pro | Leu | Val 160 |
| 50 | Gly | Met | Ala | Met | Val 165 | Pro | Ala | Leu | Leu | Gly 170 | Leu | Ile | Gly | Tyr | His 175 | Leu |
| 50 | Tyr | Arg | Lys | Ala 180 | Asn | Arg | Pro | Lys | Val 185 | Ser | Lys | Lys | Lys | Leu 190 | Lys | Glu |
| 55 | Glu | Lys | Arg 195 | Asn | Lys | Ser | Lys | Lys 200 | Lys | Xaa | | | | | | |
| | (2) | INF | ORMA' | TION | FOR | SEQ | ID | NO: | 141: | | | | | | | |

| | | | (i) S | (| ENCE A) L B) T | ENGT | H: 2 | 17 a | mino | | ds | | | | | |
|----|------------|------------|------------|------------|-------------------------|------------|------------|------------|------------|------------|------------|---------------|------------|------------|------------|------------|
| 5 | | | (xi) | (| D) TO | OPOL | OGY : | lin | ear | EQ II | ON C | : 14: | 1: | | | |
| | Met 1 | Phe | Leu | Arg | Leu 5 | Tyr | Leu | Ile | Ala | Arg 10 | Val | Met | Leu | Leu | His 15 | Ser |
| 10 | Lys | Leu | Phe | Thr 20 | Asp | Ala | Ser | Ser | Arg 25 | Ser | Ile | Gly | Ala | Leu 30 | Asn | Lys |
| 15 | Ile | Asn | Phe 35 | Asn | Thr | Arg | Phe | Val 40 | Met | Lys | Thr | Leu | Met 45 | Thr | Ile | Cys |
| | Pro | Gly 50 | Thr | Val | Leu | Leu | Val 55 | Phe | Ser | Ile | Ser | Leu 60 | Trp | Ile | Ile | Ala |
| 20 | Ala 65 | Trp | Thr | Val | Arg | Val 70 | Cys | Glu | Ser | Pro | Glu 75 | Ser | Pro | Ala | Gln | Pro 80 |
| | Ser | Gly | Ser | Ser | Leu 85 | Pro | Ala | Trp | Tyr | His 90 | Asp | Gln | Gln | Asp | Val 95 | Thr |
| 25 | Ser | Asn | Phe | Leu 100 | Gly | Ala | Met | Trp | Leu 105 | Ile | Ser | Ile | Thr | Phe 110 | Leu | Ser |
| 30 | Ile | Gly | Туr 115 | Gly | Asp | Met | Val | Pro 120 | His | Thr | Tyr | Cys | Gly 125 | Lys | Gly | Val |
| | Cys | Leu 130 | Leu | Thr | Gly | Ile | Met 135 | Gly | Ala | Gly | Cys | Thr 140 | Ala | Leu | Val | Val |
| 35 | Ala 145 | Val | Val | Ala | Arg | Lys 150 | Leu | Glu | Leu | Thr | Lys 155 | Ala | Glu | Lys | His | Val 160 |
| | His | Asn | Phe | Met | Met 165 | Asp | Thr | Gln | Leu | Thr 170 | Lys | Arg | Ile | Lys | Asn 175 | Ala |
| 40 | Ala | Ala | Asn | Val 180 | Leu | Arg | Glu | Thr | Trp 185 | Leu | Ile | Tyr | Lys | His 190 | Thr | Lys |
| 45 | Leu | Leu | Lys 195 | Lys | Ile | Asp | | Ala 200 | _ | Val | Arg | _ | His 205 | Gln | Arg | Lys |
| | Phe | Leu 210 | | Ser | Tyr | Pro | Pro 215 | Val | Xaa | | | | | | | |
| 50 | (2) | INF | ORMA' | TION | FOR | SEQ | ID | NO: | 142: | | | | | | | |
| | | | (i) | | ENCE | | | | | | .ds | | | | | |
| 55 | | | (xi) | (| (B) I (D) I OUENC | OPOL | .OGY : | lir | ear | EQ I | D NC |): 1 4 | 2: | | | |
| 60 | Met 1 | | | | Thr 5 | Val | | | | | Gln | | | Ser | Asp 15 | Ser |

| | Met | Val | Gly | Туr 20 | Val | Leu | Gly | Pro | Phe 25 | Phe | Leu | Ile | Thr | Leu 30 | Val | Gly |
|----|--|-----------|-----------|------------|----------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-----------|------------|-----------|-----------|
| 5 | Val | Val | Val 35 | Ala | Val | Val | Met | Tyr 40 | Val | Gln | Lys | Lys | Lys 45 | Arg | Val | Asp |
| 10 | Arg | Leu 50 | Arg | His | His | Leu | Leu 55 | Pro | Met | Tyr | Ser | Tyr 60 | Asp | Pro | Ala | Glu |
| | Glu 65 | Leu | His | Glu | Ala | Glu 70 | Gln | Glu | Leu | Leu | Ser 75 | Asp | Met | Gly | Asp | Pro 80 |
| 15 | Lys | Val | Val | His | Gly 85 | Trp | Gln | Ser | Gly | Tyr 90 | Gln | His | Lys | Arg | Met 95 | Pro |
| | Leu | Leu | Asp | Val 100 | Lys | Thr | | | | | | | | | | |
| 20 | | | | | | | | | | | | | | | | |
| | (2) | INF | | | FOR | | | | | | | | | | | |
| 25 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 112 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143: | | | | | | | | | | | | | | | |
| 30 | Met 1 | Arg | Glu | Cys | Gln 5 | Glu | Glu | Ser | Phe | Trp | Lys | Arg | Ala | Leu | Pro 15 | Phe |
| 35 | Ser | Leu | Val | Ser 20 | Met | Leu | Val | Thr | Gln 25 | Gly | Leu | Val | Tyr | Gln 30 | Gly | Tyr |
| | Leu | Ala | Ala 35 | Asn | Ser | Arg | Phe | Gly 40 | Ser | Leu | Pro | Lys | Val 45 | Ala | Leu | Ala |
| 40 | Gly | Leu 50 | | Gly | Phe | Gly | Leu 55 | Gly | Lys | Val | Ser | Tyr 60 | Ile | Gly | Val | Суѕ |
| | Gln 65 | | Lys | Phe | His | Phe 70 | Phe | Glu | Asp | Gln | Leu 75 | Arg | Gly | Ala | Gly | Phe 80 |
| 45 | Gly | Pro | Gln | His | Asn 85 | Arg | His | Cys | Leu | Leu 90 | Thr | Cys | Glu | Glu | Cys 95 | Lys |
| 50 | Ile | Lys | His | Gly 100 | Leu | Ser | Glu | Lys | Gly 105 | Asp | Ser | Gln | Pro | Ser 110 | Ala | Ser |
| 55 | (2) | INF | | | FOR ENCE | _ | | | | i: | | | | | | |
| 60 | | | • | | (A) I (B) T | ENGT | TH: 2 | 20 an | nino | | ls | | | | | |

(D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144: Met Lys Asn Asp Arg Asn Gln Gly Phe Ser Leu Leu Gln Leu Ile Asp 5 Trp Asn Lys Pro 10 (2) INFORMATION FOR SEQ ID NO: 145: (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145: 20 Met Gly Thr Gln Pro Pro Val Val Ala Gly Phe Thr Ile Pro Met Leu 10 5 Gly Tyr Thr Val Arg Val Leu Thr Phe His Leu Ser Cys Ser 20 25 25 (2) INFORMATION FOR SEQ ID NO: 146: 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 99 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146: 35 Met Lys Ile Pro Val Leu Pro Ala Val Val Leu Leu Ser Leu Leu Val Leu His Ser Ala Gln Gly Ala Thr Leu Gly Gly Pro Glu Glu Glu Ser 40 Thr Ile Glu Asn Tyr Ala Ser Arg Pro Glu Ala Phe Asn Thr Pro Phe Leu Asn Ile Asp Lys Leu Arg Ser Ala Phe Lys Ala Asp Glu Phe Leu 45 Asn Trp His Ala Leu Phe Glu Ser Ile Lys Arg Lys Leu Pro Phe Leu 75 50 Asn Trp Asp Ala Phe Pro Lys Leu Lys Gly Leu Arg Ser Ala Thr Pro 90 Asp Ala Gln 55 (2) INFORMATION FOR SEQ ID NO: 147: 60

```
(i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 8 amino acids
                    (B) TYPE: amino acid
                    (D) TOPOLOGY: linear
 5
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:
     Met Val Trp Gly Leu Leu Leu Gly
10
      (2) INFORMATION FOR SEQ ID NO: 148:
             (i) SEQUENCE CHARACTERISTICS:
15
                    (A) LENGTH: 39 amino acids
                    (B) TYPE: amino acid
                    (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:
20
      Met Leu Pro Leu Leu Ser Leu Leu Phe Leu Phe Ser Thr Val Ser
               5
                                         10
      Ser Phe Cys Gly Met Pro Leu Arg Ala His Thr Arg Ala Xaa Ala His
                  20
                                      25
25
      Thr Arg Thr Phe Ala Ser Arg
              35
30
      (2) INFORMATION FOR SEQ ID NO: 149:
             (i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 131 amino acids
35
                    (B) TYPE: amino acid
                    (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:
      Met Ile Cys Glu Thr Lys Ala Arg Lys Ser Ser Gly Gln Pro Gly Arg
40
      Leu Pro Pro Pro Thr Leu Ala Pro Pro Gln Pro Pro Leu Pro Glu Thr
45
      Ile Glu Arg Pro Val Gly Thr Gly Ala Met Val Ala Arg Ser Ser Asp
      Leu Pro Tyr Leu Ile Val Gly Val Leu Gly Ser Ile Val Leu Ile
50
      Ile Val Thr Phe Ile Pro Phe Cys Leu Trp Arg Ala Trp Ser Lys Gln
      Lys His Thr Thr Asp Leu Gly Phe Pro Arg Ser Ala Leu Pro Pro Ser
55
                                           90
      Cys Pro Tyr Thr Met Val Pro Leu Gly Gly Leu Pro Gly His Gln Ala
                  100
                                      105
60
      Val Asp Ser Pro Thr Ser Val Ala Ser Val Asp Gly Pro Val Leu Met
```

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115 120 125 Gly Ser Thr 130 5 (2) INFORMATION FOR SEQ ID NO: 150: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150: 15 Met Gly Ala Pro Ser Leu Thr Met Leu Leu Leu Leu Lys Val Gln Pro Arg Arg Thr Gln Ala Phe Asp Ala His Trp Val Gly Leu Pro Leu Leu 20 25 20 25 (2) INFORMATION FOR SEQ ID NO: 151: (i) SEQUENCE CHARACTERISTICS: 30 (A) LENGTH: 14 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151: Met Cys Leu Ile Phe Leu Leu Leu Leu Leu Ser Phe Ser 35 1 5 40 (2) INFORMATION FOR SEQ ID NO: 152: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 8 amino acids (B) TYPE: amino acid 45 (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152: His Pro His Gln Asp Ser Gln Pro 5 50 (2) INFORMATION FOR SEQ ID NO: 153: 55 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 68 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153: 60

| | Met 1 | Asn | Thr | Ser | Tyr 5 | Ile | Leu | Arg | Leu | Thr 10 | Val | Val | Val | Ser | Val 15 | Val |
|----|-----------|-----------|-------------|-----------|--------------|--------------|--------------|---------------|--------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| .5 | Ile | Tyr | Leu | Ala 20 | Ile | His | Pro | Leu | Leu 25 | Ser | Phe | Ser | Leu | Glu 30 | Ser | Pro |
| | Leu | Leu | Val 35 | Pro | Trp | Arg | Asp | Cys 40 | Cys | Gln | Asn | Ile | Trp 45 | Lys | Ser | Gly |
| 10 | Ser | Val 50 | Trp | Tyr | Lys | Arg | Trp 55 | Thr | Leu | Pro | His | Met 60 | Glu | Val | Cys | Cys |
| 15 | Gln 65 | Asp | Leu | His | | | | | | | | | | | | |
| 20 | (2) | | ORMAT | SEQUI | ENCE A) L | CHAI | RACT H: 2 | ERIS' 6 am | TICS ino | : acid | s | | | | | |
| 25 | Met | | (xi) Lys | SEQ | D) T UENC | OPOL | OGY: SCRI | lin PTIO | ear N: S | | | | | Ile | Leu | Thr |
| 30 | 1 Ser | Ile | Arg | Ile 20 | 5 Leu | Glu | Arg | Gln | Asn 25 | 10 Met | | | | | 15 | |
| 35 | (2) | INF | ORMAT | SEQU (| ENCE A) L | CHA | RACT | ERIS 95 a | TICS mino | : aci | ds | | | | | |
| 40 | | | (xi) | | | OPOL E DE | | | | EQ I | D NO | : 15 | 5: | | | |
| | Met 1 | Asp | Cys | Glu | Val 5 | Asn | Asn | Gly | Ser | Ser 10 | Leu | Arg | Asp | Glu | Cys 15 | Ile |
| 45 | Thr | Asn | Leu | Leu 20 | Val | Phe | Gly | Phe | Leu 25 | Gln | Ser | Суз | Ser | Asp 30 | Asn | Ser |
| 50 | Phe | Arg | Arg 35 | Glu | Leu | Asp | Ala | Leu 40 | Gly | His | Glu | Leu | Pro 45 | Val | Leu | Ala |
| 50 | Pro | Gln 50 | Trp | Glu | Gly | Tyr | Asp 55 | Glu | Leu | Gln | Thr | Asp 60 | Gly | Asn | Arg | Ser |
| 55 | Ser 65 | | Ser | Arg | Leu | Gly 70 | Arg | Ile | Glu | Ala | Asp 75 | Ser | Glu | Ser | Gln | Glu 80 |
| | Asp | Ile | Ile | Arg | Asn 85 | Ile | Ala | Arg | His | Leu 90 | Ala | Gln | Val | Gly | Asp 95 | Ser |
| 60 | Met | Asp | Arg | Ser | Ile | Pro | Pro | Gly | Leu | Val | Asn | Gly | Leu | Ala | Leu | Gln |

| | | | | 100 | | | | | 105 | | | | | 110 | | |
|----|------------|------------|------------|---------------------|------------------------------|--------------------------|-----------------------------|-------------------------------|---------------------------|------------|------------|---------------|------------|------------|------------|------------|
| 5 | Leu | Arg | Asn 115 | Thr | Ser | Arg | Ser | Glu 120 | Glu | Asp | Arg | Asn | Arg 125 | Asp | Leu | Ala |
| 3 | Thr | Ala 130 | Leu | Glu | Gln | Leu | Leu 135 | Gln | Ala | Tyr | Pro | Arg 140 | Asp | Met | Glu | Lys |
| 10 | Glu 145 | Lys | Thr | Met | Leu | Val 150 | Leu | Ala | Leu | Leu | Leu 155 | Ala | Lys | Lys | Val | Ala 160 |
| | Ser | His | Thr | Pro | Ser 165 | Leu | Leu | Arg | Asp | Val 170 | Phe | His | Thr | Thr | Val 175 | Asn |
| 15 | Phe | Ile | Asn | Gln 180 | Asn | Leu | Arg | Thr | Туг 185 | Val | Arg | Ser | Leu | Ala 190 | Arg | Asn |
| 20 | Gly | Met | Asp 195 | | | | | | | | | | | | | |
| 25 | (2) | INF | (i) | SEQU)) (| ENCE A) L B) T D) T | CHA ENGT YPE: | RACT H: 9 ami OGY: | NO: I ERIS 1 am no a lin PTIO | TICS ino cid ear | acid | | : 15 | 6: | | | |
| 30 | Met 1 | Ser | | | | | | | | | | | Ser | Thr | Leu 15 | Ala |
| 35 | Cys | Ser | Phe | Leu 20 | Arg | Pro | Lys | Ala | Arg 25 | Pro | Ser | Lys | Arg | Ser 30 | Pro | Arg |
| | Asn | Tyr | Thr 35 | | Ser | Thr | Ser | Pro 40 | Gly | Gly | Pro | Arg | Ala 45 | Pro | Arg | Gly |
| 40 | Gly | Ala 50 | | Arg | Leu | Ser | Ser 55 | | Gln | Asn | Ser | Ser 60 | Pro | Lys | Gly | Val |
| 45 | Ala 65 | Val | Ala | Lys | Ala | Ser 70 | _ | Arg | Pro | Val | Leu 75 | | Phe | Leu | Pro | Gly 80 |
| | Pro | Trp | Ser | Ser | Xaa 85 | Pro | Xaa | Ala | Phe | Leu 90 | | | | | | |
| 50 | (2) | INF | 'ORMA | MOIT | FOR | SEQ | ID | NO: | 157: | | | | | | | |
| 55 | | | | | (A) I (B) I (D) I | LENGT TYPE : TOPOI | TH: 1 : am: LOGY | TERIS Ino a Ino a IPTIC | mino acid near | acio | |): 1 5 | 57 : | | | ٠ |
| 60 | Met | Gly | Thr | Leu | Ser | | Glu | Cys | Ser | Gly | | Ala | Thr | Leu | Gly | |

| | Cys | Leu | Val | Val 20 | Pro | Trp | Asn | Ser | Ser 25 | Gly | Leu | Ser | Gln | Pro 30 | Pro | |
|----|-----------|-----------|-----------|-----------|-------------------------|-----------------------|----------------------|---------------------------------------|---------------------|-----------|-----------|---------------|-----------|-----------|-----------|-----------|
| 5 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA' | TION | FOR | SEQ | ID N | 10: 1 | 158: | | | | | | | |
| 10 | | | | (| A) L B) T D) T | ENGT: YPE: OPOL | H: 9 ami: OGY: | ERIST 1 am no a lind PTIO | ino a cid ear | acid | | : 15 | 8: | | | |
| 15 | Met 1 | Lys | Phe | Leu | Ala 5 | Val | Leu | Val | Leu | Leu 10 | Gly | Val | Ser | Ile | Phe 15 | Leu |
| 20 | Val | Ser | Ala | Gln 20 | Asn | Pro | Thr | Thr | Ala 25 | Ala | Pro | Ala | Asp | Thr 30 | Tyr | Pro |
| 20 | Ala | Thr | Gly 35 | | Ala | Asp | Asp | Glu 40 | Ala | Pro | Asp | Ala | Glu 45 | Thr | Thr | Ala |
| 25 | Ala | Ala 50 | | Thr | Ala | Thr | Thr 55 | Ala | Ala | Pro | Thr | Thr 60 | Ala | Thr | Thr | Ala |
| | Ala 65 | | Thr | Thr | Ala | Arg 70 | Lys | Asp | Ile | Pro | Val 75 | Leu | Pro | Lys | Trp | Val 80 |
| 30 | Gly | Asp | Leu | Pro | Asn 85 | Gly | Arg | Val | Cys | Pro 90 | Xaa | | | | | |
| 35 | (2) | INF | ORMA | MOIT | FOR | SEQ | ID : | NO: | 159: | | | | | | | |
| 40 | | | | | (A) I (B) T (D) T | ENGI YPE : OPOI | TH: 8 ami | ERIS 39 am ino a 1 lin | nino cid near | acid | | o: 1 5 | 9 : | | | |
| 15 | Met 1 | | e Il∈ | e Ser | Leu 5 | | Ile | Tyr | Ile | Phe 10 | | Thr | Cys | Ser | Asn 15 | Thr |
| 45 | Ser | Pro | Ser | 7 Tyr | | Gly | Thr | Gln | Leu 25 | | Leu | Gly | Leu | Pro 30 | | Ala |
| 50 | Glr | Tr | Try | | Leu | Thr | Gly | Arg 40 | | Met | Gln | Cys | Cys 45 | | Leu | Phe |
| | Суз | Phe 50 | | ı Lev | ı Glm | . Asn | Cys 55 | Leu | Phe | Pro | Phe | Pro 60 | | His | Leu | Ile |
| 55 | Glr 65 | | s Ası | o Pro | Cys | Glu 70 | | ı Val | . Leu | Thr | 75 | | Trp | Asp | Trp | Ala 80 |
| 60 | Glı | ı Ala | a Gly | y Alá | a Ser 85 | | і Туі | : Ser | Pro | > | | | | | | |

| | (2) | INFO | ORMAT | NOI | FOR | SEQ | ID N | 10: 1 | 60: | | | | | | | |
|----------|------------|------------|------------|------------|--------------|-------------------------------|-------------|------------|-------------|------------|------------|------------|------------|------------|-----------|------------|
| 5 | | | (i) S | - (. (: | A) L B) T | CHAI ENGT: YPE: OPOL | H: 1 ami | 74 ar | mino cid | | ds | | | | | |
| | | | (xi) | | - | | | | | EQ II | OM C | : 160 | 0: | | | |
| 10 | Met 1 | Ser | Ser | Ala | Ala 5 | Ala | Asp | His | Trp | Ala 10 | Trp | Leu | Leu | Val | Leu 15 | Ser |
| 15 | Phe | Val | Phe | Gly 20 | Cys | Asn | Val | Leu | Arg 25 | Ile | Leu | Leu | Pro | Ser 30 | Phe | Ser |
| | Ser | Phe | Met 35 | Ser | Arg | Val | Leu | Gln 40 | Lys | Asp | Ala | Glu | Gln 45 | Glu | Ser | Gln |
| 20 | Met | Arg 50 | Ala | Glu | Ile | Gln | Asp 55 | Met | Lys | Gln | Glu | Leu 60 | Ser | Thr | Val | Asn |
| 25 | Met 65 | Met | Asp | Glu | Phe | Ala 70 | Arg | Tyr | Ala | Arg | Leu 75 | Glu | Arg | Lys | Ile | Asn 80 |
| | Lys | Met | Thr | Asp | Lys 85 | Leu | Lys | Thr | His | Val 90 | Lys | Ala | Arg | Thr | Ala 95 | Gln |
| 30 | Leu | Ala | Lys | Ile 100 | Lys | Trp | Val | Ile | Ser 105 | Val | Ala | Phe | Tyr | Val 110 | Leu | Glr |
| | Ala | Ala | Leu 115 | Met | Ile | Ser | Leu | 11e 120 | Trp | Lys | Tyr | Tyr | Ser 125 | Val | Pro | Val |
| 35 | Ala | Val 130 | Val | Pro | Ser | Lys | Ттр 135 | Ile | Thr | Pro | Leu | Asp 140 | Arg | Leu | Val | Alā |
| 40 | Phe 145 | | Thr | Arg | Val | Ala 150 | Gly | Gly | Val | Gly | Ile 155 | Thr | Cys | Trp | Ile | Let 160 |
| •• | Val | Cys | Asn | Lys | Val 165 | | Ala | Ile | Val | Leu 170 | His | Pro | Phe | Ser | | |
| 45 | (2) | INF | 'ORMA' | TION | FOR | . SEQ | ID | NO: | 161: | | | | | | | |
| . | | | (i) | | | CHA | | | | | ls | | | | | |
| 50 | | | (xi) | | (D) : | TYPE: TOPOI SE DE | OGY: | lir | ıear | SEQ I | D NC |): 16 | 51: | | | |
| 55 | Met 1 | | , Lys | Leu | ı Ile | | Ile | · Val | Ile | Arg | | Pro | Leu | Leu | Leu 15 | |
| | Leu | ı Val | Gln | Cys 20 | | ı Asn | Cys | Cys | Arg | | Asn | Met | . Leu | Туг 30 | | 11 |
| 60 | Phe | - J.e. |) Asn | T16 | • His | : Asr | 116 | . His | Lvs | : Phe | Ser | Asr | . His | : | | |

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35 40 45 5 (2) INFORMATION FOR SEQ ID NO: 162: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids (B) TYPE: amino acid 10 (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162: Met Val Ala Ser Thr Leu Val Thr Asn Leu Phe Gly Val Ala Phe Ala 10 15 Thr Thr Ala Ala Thr Arg Ala 20 20 (2) INFORMATION FOR SEQ ID NO: 163: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 70 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163: Met Leu Met Ala Pro Val Val Cys Leu Ser Phe Ser Pro Cys Pro Ala 30 Asp Thr Ser Leu Thr Gly Asp Gly Leu Lys Ala Gly Leu Glu Arg Gly 35 Xaa Ala Leu Val Thr Leu Phe Asp Ser Val Thr His Phe Leu Ala His Thr Leu Phe Glu Leu Leu Asp Phe Gln Leu Ala Phe Leu Arg Ser Gly 55 40 Lys Gln Thr Ala Pro His 65 45 (2) INFORMATION FOR SEQ ID NO: 164: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 323 amino acids 50 (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164: Met Leu Leu Leu Leu Leu Gly Ser Gly Gln Gly Pro Gln Gln 55 5 1 10 Val Gly Ala Gly Gln Thr Phe Glu Tyr Leu Lys Arg Glu His Ser Leu

Ser Lys Pro Tyr Gln Gly Val Gly Thr Gly Ser Ser Ser Leu Trp Asn

| | | | 35 | | | | | 40 | | | | | 45 | | | |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Leu | Met 50 | Gly | Asn | Ala | Met | Val 55 | Met | Thr | Gln | Tyr | Ile 60 | Arg | Leu | Thr | Pro |
| J | Asp 65 | Met | Gln | Ser | Lys | Gln 70 | Gly | Ala | Leu | Trp | Asn 75 | Arg | Val | Pro | Cys | Phe 80 |
| 10 | Leu | Arg | Asp | Trp | Glu 85 | Leu | Gln | Val | His | Phe 90 | Lys | Ile | His | Gly | Gln 95 | Gly |
| | Lys | Lys | Asn | Leu 100 | His | Gly | Asp | Gly | Leu 105 | Ala | Ile | Trp | Tyr | Thr 110 | Arg | Asn |
| 15 | Arg | Met | Gln 115 | Pro | Gly | Pro | Val | Phe 120 | Gly | Asn | Met | Asp | Lys 125 | Phe | Val | Gly |
| 20 | Leu | Gly 130 | Val | Phe | Val | Asp | Thr 135 | Tyr | Pro | Asn | Glu | Glu 140 | Lys | Gln | Gln | Glu |
| | Arg 145 | Val | Phe | Pro | Tyr | 11e 150 | Ser | Ala | Met | Val | Asn 155 | Asn | Gly | Ser | Leu | Ser 160 |
| 25 | Tyr | Asp | His | Glu | Arg 165 | Asp | Gly | Arg | Pro | Thr 170 | Glu | Leu | Gly | Gly | Cys 175 | Thr |
| | Ala | Ile | Val | Arg 180 | Asn | Leu | His | Tyr | Asp 185 | Thr | Phe | Leu | Val | Ile 190 | Arg | Tyr |
| 30 | Val | Lys | Arg 195 | His | Leu | Thr | Ile | Met 200 | Met | Asp | Ile | Asp | Gly 205 | Lys | His | Glu |
| 35 | Trp | Arg 210 | Asp | Cys | Ile | Glu | Val 215 | Pro | Gly | Val | Arg | Leu 220 | Pro | Arg | Gly | Tyr |
| | 225 | | | | | 230 | | Thr | | | 235 | | | | | 240 |
| 40 | Val | Ile | Ser | Leu | Lys 245 | Leu | Phe | Glu | Leu | Thr 250 | Val | Glu | Arg | Thr | Pro 255 | Glu |
| | Glu | Glu | Lys | Leu 260 | | Arg | Asp | Val | Phe 265 | Leu | Pro | Ser | Val | Asp 270 | Asn | Met |
| 45 | Lys | Leu | Pro 275 | | Met | Thr | Ala | Pro 280 | | Pro | Pro | Leu | Ser 285 | Gly | Leu | Ala |
| 50 | Leu | Phe 290 | | Ile | Val | Phe | Phe 295 | Ser | Leu | Val | Phe | Ser 300 | | Phe | Ala | Ile |
| | Val 305 | | Gly | Ile | Ile | Leu 310 | | Asn | Lys | Trp | Gln 315 | | Gln | Ser | Arg | Lys 320 |
| 55 | Arg | Phe | Tyr | | | | | | | | | | | | | |
| (0 | (2) | INF | 'ORMA | MOIT | FOR | SEQ | OI Q | NO: | 165: | | | | | | | |
| 60 | | | | | | | | | | | | | | | | |

| | | | (i) | (| A) L B) T | ENGT YPE : | H: 3 ami | ERIS' 21 a no a lin | mino cid | | ds | | | | | |
|----|------------|------------|------------|------------|--------------|---------------|-------------|------------------------------|-------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | | | (xi) | SEQ | | | | | | EQ II | D NO | : 16 | 5: | | | |
| | Met 1 | Pro | Ser | Glu | Tyr 5 | Thr | Tyr | Val | Lys | Leu 10 | Arg | Ser | Asp | Cys | Ser 15 | Arg |
| 10 | Pro | Ser | Leu | Gln 20 | Trp | Tyr | Thr | Arg | Ala 25 | Gln | Ser | Lys | Met | Arg 30 | Arg | Pro |
| 15 | Ser | Leu | Leu 35 | Leu | Lys | Asp | Ile | Leu 40 | Lys | Cys | Thr | Leu | Leu 45 | Val | Phe | Gly |
| 13 | Val | Trp 50 | Ile | Leu | Tyr | Ile | Leu 55 | Lys | Leu | Asn | Tyr | Thr 60 | Thr | Glu | Glu | Cys |
| 20 | Asp 65 | Met | Lys | Lys | Met | His 70 | Tyr | Val | Asp | Pro | Asp 75 | His | Val | Lys | Arg | Ala 80 |
| | Gln | Lys | Tyr | Ala | Gln 85 | Gln | Val | Leu | Gln | Lys 90 | Glu | Cys | Arg | Pro | Lys 95 | Phe |
| 25 | Ala | Lys | Thr | Ser 100 | Met | Ala | Leu | Leu | Phe 105 | Glu | His | Arg | Tyr | Ser 110 | Val | Asp |
| 30 | Leu | Leu | Pro 115 | Phe | Val | Gln | Lys | Xaa 120 | Pro | Lys | Asp | Ser | Glu 125 | Ala | Glu | Ser |
| 50 | Lys | Tyr 130 | Asp | Pro | Pro | Phe | Gly 135 | Phe | Arg | Lys | Phe | Ser 140 | Ser | Lys | Val | Gln |
| 35 | Thr 145 | Leu | Leu | Glu | Leu | Leu 150 | Pro | Glu | His | Asp | Leu 155 | Pro | Glu | His | Leu | Lys 160 |
| | Ala | Lys | Thr | Cys | Arg 165 | Arg | Cys | Val | Val | Ile 170 | Gly | Ser | Gly | Gly | Ile 175 | Leu |
| 40 | His | Gly | Leu | Glu 180 | Leu | Gly | His | Thr | Leu 185 | Asn | Gln | Phe | Asp | Val 190 | Val | Ile |
| 45 | Arg | Leu | Asn 195 | Ser | Ala | Pro | Val | Glu 200 | Gly | Tyr | Ser | Glu | His 205 | Val | Gly | Asn |
| 15 | Lys | Thr 210 | Thr | Ile | Arg | Met | Thr 215 | Tyr | Pro | Glu | Gly | Ala 220 | Pro | Leu | Ser | Asp |
| 50 | Leu 225 | Glu | Tyr | Tyr | Ser | Asn 230 | Asp | Leu | Phe | Val | Ala 235 | Val | Leu | Phe | Lys | Ser 240 |
| | Val | Asp | Phe | Asn | Trp 245 | Leu | Gln | Ala | Met | Val 250 | Lys | Lys | Glu | Thr | Leu 255 | Pro |
| 55 | Phe | Trp | Val | Arg 260 | Leu | Phe | Phe | Trp | Lys 265 | | Val | Ala | Glu | Lys 270 | Ile | Pro |
| 60 | Leu | Gln | Pro 275 | Lys | His | Phe | Arg | Ile 280 | Leu | Asn | Pro | Val | Ile 285 | Ile | Lys | Glu |

| | Thr | Ala 290 | Phe | Xaa | His | Pro | Ser 295 | Val | Leu | Arg | Ala | Ser 300 | Val | Lys | Val | Leu |
|----|------------|------------|-----------|----------------|----------------------|----------------------|---------------------|---------------------------------------|--------------------|-----------|------------|-------------|-----------|-----------|-----------|------------|
| 5 | Gly 305 | Ala | Glu | Ile | Arg | Thr 310 | Ser | Pro | Gln | Ser | Val 315 | Ser | Leu | Pro | Leu | Ser 320 |
| | Xaa | | | | | | | | | | | | | | | |
| 10 | | | | | | | | | | | | | | | | |
| 15 | (2) | INF | | SEQU)) | ENCE A) L B) T | CHAI ENGT YPE: | RACT H: 3 ami | NO: 1 ERIS' 1 am no a lin | FICS ino cid | | s | | | | | |
| | | | | SEQ | UENC: | E DE | SCRI | PTIO | N: S | | | | | | | |
| 20 | Met 1 | Thr | Leu | Asp | Val 5 | Gln | Thr | Val | Val | Val 10 | Phe | Ala | Val | Ile | Val 15 | Val |
| 25 | Leu | Leu | Leu | Val 20 | Asn | Val | Ile | Leu | Met 25 | Phe | Phe | Leu | Gly | Thr 30 | Arg | |
| | (2) | INF | ORMA' | TION | FOR | SEQ | ID I | NO: | 167: | | | | | | | |
| 30 | | | (i) | (| (A) L (B) T | ENGT YPE : | H: 7 ami | ERIS 2 am no a lin | ino cid | | ls | | | | | |
| 35 | | | | _ | | | | PTIO | | | | | | 7 | G1 | D |
| | Met 1 | | Pro | Leu | Leu 5 | Phe | Cys | Ala | Pne | 10 | | His | Lys | ьеu | 15 | |
| 40 | Leu | Leu | Phe | Leu 20 | | Asp | Val | Leu | Met 25 | | His | Glu | Ala | Val 30 | Met | Arg |
| | Thr | His | Gln 35 | | Gln | Leu | Pro | Asp 40 | | Glu | Phe | Pro | Ser 45 | Gln | Gln | Asn |
| 45 | Gln | Val 50 | | Asn | Lys | Thr | Leu 55 | Phe | Asn | Lys | Leu | . Lys 60 | | Lys | Lys | Lys |
| 50 | Lys 65 | _ | : Lys | Xaa | Xaa | . Xaa 70 | | Lys | | | | | | | | |
| | (2) | INF | FORMA | MOIT | FOR | SEÇ | ID | NO: | 168: | | | | | | | |
| 55 | | | (i) | - | (A) 1 (B) 1 | LENG TYPE | TH: : | reris 282 a ino a : lin | amino acid | | ids | | | | | |
| 60 | | | (xi) |) SE(| | | | IPTIC | | SEQ : | ID NO |): 16 | 58: | | | |

| | Met 1 | Ala | Ser | Arg | Gly 5 | Arg | Arg | Pro | Glu | His 10 | Gly | Gly | Pro | Pro | Glu 15 | Let |
|-----|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------------|-----------------|
| 5 | Phe | Tyr | Asp | Glu 20 | Thr | Glu | Ala | Arg | Lys 25 | Tyr | Val | Arg | Asn | Ser 30 | Arg | Met |
| | Ile | Asp | 11e 35 | Gln | Thr | Arg | Met | Ala 40 | Gly | Arg | Ala | Leu | Glu 45 | Leu | Leu | Туі |
| 10 | Leu | Pro 50 | Glu | Asn | Lys | Pro | Cys 55 | Tyr | Leu | Leu | Asp | Ile 60 | Gly | Cys | Gly | Thi |
| 15 | Gly 65 | Leu | Ser | Gly | Ser | Tyr 70 | Leu | Ser | Asp | Glu | Gly 75 | His | Tyr | Trp | Val | Gl ₂ |
| | Leu | Asp | Ile | Ser | Pro 85 | Ala | Met | Leu | Asp | Glu 90 | Ala | Val | Asp | Arg | Glu 95 | Ile |
| 20 | Glu | Gly | Asp | Leu 100 | Leu | Leu | Gly | Asp | Met 105 | Gly | Gln | Gly | Ile | Pro 110 | Phe | Lys |
| | Pro | Gly | Thr 115 | Phe | Asp | Gly | Cys | Ile 120 | Ser | Ile | Ser | Ala | Val 125 | Gln | Trp | Leu |
| 25 | Cys | Asn 130 | Ala | Asn | Lys | Lys | Ser 135 | Glu | Asn | Pro | Ala | Lys 140 | Arg | Leu | Tyr | Суя |
| 30 | Phe 145 | Phe | Ala | Ser | Leu | Phe 150 | Ser | Val | Leu | Val | Arg 155 | Gly | Ser | Arg | Ala | Va] |
| | Leu | Gln | Leu | Tyr | Pro 165 | Glu | Asn | Ser | Glu | Gln 170 | Leu | Glu | Leu | Ile | Thr 175 | Thi |
| 35 | Gln | Ala | Thr | Lys 180 | Ala | Gly | Phe | Ser | Gly 185 | Gly | Met | Val | Val | Asp 190 | Tyr | Pro |
| | Asn | Ser | Ala 195 | Lys | Ala | Lys | Lys | Phe 200 | Tyr | Leu | Cys | Leu | Phe 205 | Ser | Gly | Pro |
| 40 | Ser | Thr 210 | Phe | Ile | Pro | Glu | Gly 215 | Leu | Ser | Glu | Asn | Gln 220 | Asp | Glu | Val | Glu |
| 45 | Pro 225 | Arg | Glu | Ser | Val | Phe 230 | Thr | Asn | Glu | Arg | Phe 235 | Pro | Leu | Arg | Met | Ser 240 |
| ,,, | Arg | Arg | Gly | Met | Val 245 | Arg | Lys | Ser | Arg | Ala 250 | Trp | Val | Leu | Glu | Lys 255 | Lys |
| 50 | Glu | Arg | His | Arg 260 | Arg | Gln | Gly | Arg | Glu 265 | Val | Arg | Pro | Asp | Thr 270 | Gln | Туз |
| | Thr | Gly | Arg 275 | Lys | Arg | Lys | Pro | Arg 280 | Phe | Хаа | | | | | | |
| 55 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA' | rion | FOR | SEQ | ID I | 10: . | 169: | | | | | | | |
| 60 | | | (i) | | | CHA ENGT | | | | | s | | | | | |

| | | | | | | | | no ac | | | | | | | | |
|-----|----------|-----------|-----------|------------|-------------------------------|--------------------------------|--------------------------------|---------------------------------|-----------------------------|-----------|-----|-----------|------------|-----------|-----------|-----|
| | | 1 | (xi) | SEQU | | | | line TION | | EO II | NO: | : 169 |): | | | |
| 5 | Met 1 | | | Lys | | | | | | | | | | Ser | Arg 15 | Lys |
| 10 | | Met | Val | Cys 20 | | Ser | Thr | | | 10 | | | | | | |
| 15 | (2) | | (i) S | (1 | ENCE A) LI B) T D) T | CHAI ENGTI YPE: OPOLO | RACTI H: 3: amin OGY: | ERIST 28 ar no ac line | TICS: mino cid ear | acio | | : 170 |) : | | | |
| 20 | Met 1 | Trp | Arg | Pro | Ser 5 | Val | Leu | Leu | Leu | Leu 10 | Leu | Leu | Leu | Arg | His 15 | Gly |
| 25 | Ala | Gln | Gly | Lys 20 | Pro | Ser | Pro | Asp | Ala 25 | Gly | Pro | His | Gly | Gln 30 | Gly | Arg |
| | Val | His | Gln 35 | Ala | Ala | Pro | Leu | Ser 40 | Asp | Ala | Pro | His | Asp 45 | Asp | Ala | His |
| 30 | Gly | Asn 50 | Phe | Gln | Tyr | Asp | His 55 | Glu | Ala | Phe | Leu | Gly 60 | Arg | Glu | Val | Ala |
| 35 | 65 | | | Asp | | 70 | | | | | 75 | | | | | 80 |
| | | | | Asp | 85 | | | | | 90 | | | | | 95 | |
| 40 | | | | Glu 100 | | | | | 105 | | | | | 110 | | |
| | | | 115 | Ser | | | | 120 | | | | | 125 | | | |
| 45 | | 130 | | Val | | | 135 | | | | | 140 | | | | |
| 50 | 145 | | | Gly | | 150 | | | | | 155 | | | | | 160 |
| | | _ | | Leu | 165 | | | | | 170 | | | | | 175 | |
| 55 | | | | Ser 180 | | | | | 185 | | | | | 190 | | |
| 60 | | | 195 | | | | | 200 | | | | | 205 | | | |
| OU. | Glu | Asn | 1.011 | Asp | Ara | Asn | LVS | Asp | Giv | "የህጉ | Val | Gin | val | Glu | Glu | TV |

| | | 210 | | | | | 215 | | | | | 220 | | | | |
|----|------------|------------|------------|------------|---------------------|----------------------|-------------|--------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Ile 225 | Ala | Asp | Leu | Tyr | Ser 230 | Ala | Glu | Pro | Gly | Glu 235 | Glu | Glu | Pro | Ala | Trp 240 |
| J | Val | Gln | Thr | Glu | Arg 245 | Gln | Gln | Phe | Arg | Asp 250 | Phe | Arg | Asp | Leu | Asn 255 | Lys |
| 10 | Asp | Gly | His | Leu 260 | Asp | Gly | Ser | Glu | Val 265 | Gly | His | Trp | Val | Leu 270 | Pro | Pro |
| | Ala | Gln | Asp 275 | Gln | Pro | Leu | Val | Glu 280 | Ala | Asn | His | Leu | Leu 285 | His | Glu | Ser |
| 15 | Asp | Thr 290 | Asp | Lys | Asp | Gly | Arg 295 | Leu | Ser | Lys | Ala | Xaa 300 | Ile | Leu | Gly | Asn |
| 20 | Trp 305 | Asn | Met | Phe | Val | Gly 310 | Ser | Gln | Ala | Thr | Asn 315 | Tyr | Gly | Glu | Asp | Leu 320 |
| 20 | Thr | Arg | His | His | Asp 325 | Glu | Leu | Xaa | | | | | | | , | |
| 25 | (2) | TNF | ORMA' | MOTT | FOR | SEO | ו מד | NO · | 171 · | | | | | | | |
| | (2) | | (i) | | | _ | | | | • | | | | | | |
| 30 | | | (-) | (| A) L B) T | ENGT YPE: OPOL | H: 6 ami | 9 am no a | ino cid | | s | | | | | |
| | | | (xi) | SEQ | UENC: | E DE | SCRI | PTIO | N: S | EQ I | D NO | : 17 | 1: | | | |
| 35 | Met 1 | Cys | Trp | Leu | Arg 5 | Ala | Trp | Xaa | Gln | Ile 10 | Xaa | Leu | Pro | Val | Phe 15 | Xaa |
| | Ser | Xaa | Phe | Leu 20 | Ile | Gln | Leu | Leu | Ile 25 | Ser | Phe | Ser | Glu | Asn 30 | Gly | Phe |
| 40 | Ile | His | Ser 35 | Pro | Arg | Asn | Asn | Gln 40 | Lys | Pro | Arg | Asp | Gly 45 | Asn | Xaa | Glu |
| 45 | Glu | Cys 50 | Ala | Val | Lys | Lys | Ser 55 | Cys | Gln | Leu | Суѕ | Thr 60 | Glu | Asp | Lys | Lys |
| 43 | Туг 65 | Met | Met | Asn | Arg | | | | | | | | | | | |
| 50 | (2) | TNE | ODMA | TT ON | FOR | CEO | TD I | NO | 172. | | | | | | | |
| | (2) | INF | ORMA' | | | | | | | | | | | | | |
| 55 | | | (1) | (| A) L | CHA ENGT YPE : | н: 1 | | mino | | ds | | | | | |
| 33 | | | | | | OPOL | OGY: | lin | | | | | | | | |
| 33 | | | (xi) | (| D) I | | | | ear | EQ I | D NO | : 17 | 2: | | | |

Val Met Asp Glu Lys Val Lys Arg Ser Phe Val Leu Asp Thr Ala Ser

| | | | | 20 | | | | | 25 | | | | | 30 | | |
|------------|------------|------------|------------|------------|----------------------|---------------------|---------------------|-----------------------|--------------|-----------|------------|------------|------------|------------|-----------|------------|
| 5 | Ala | Ile | Cys 35 | Asn | Tyr | Asn | Ala | His 40 | Tyr | Lys | Asn | His | Pro 45 | Lys | Tyr | Trp |
| 10 | Cys | Arg 50 | Gly | Tyr | Phe | Arg | Asp 55 | Tyr | Cys | Asn | Ile | Ile 60 | Ala | Phe | Ser | Pro |
| 10 | Asn 65 | Ser | Thr | Asn | His | Val 70 | Ala | Leu | Lys | Asp | Thr 75 | Gly | Asn | Gln | Leu | Ile 80 |
| 15 | Val | Thr | Met | Ser | Cys 85 | Leu | Asn | Lys | Glu | Asp 90 | Thr | Gly | Trp | Tyr | Trp 95 | Cys |
| | Gly | Ile | Gln | Arg 100 | Asp | Phe | Ala | Arg | Asp 105 | Asp | Met | Asp | Phe | Thr 110 | Glu | Leu |
| 20 | Ile | Val | Thr 115 | Asp | Asp | Lys | Gly | Thr 120 | Trp | Pro | Met | Thr | Leu 125 | Val | Trp | Glu |
| 25 | Arg | Leu 130 | Ser | Gly | Thr | Lys | Pro 135 | Glu | Ala | Ala | Arg | Leu 140 | Pro | Lys | Leu | Ser |
| 4 3 | Ala 145 | Arg | Leu | Thr | Ala | Pro 150 | Gly | Arg | Pro | Phe | Ser 155 | Ser | Phe | Ala | Tyr | Xaa 160 |
| 30 | | | | | | | | | | | | | | | | |
| 35 | (2) | INF | | SEQU (| ENCE A) L B) T | CHA ENGT YPE: | RACT H: 1 ami | NO: : ERIS .23 a no a | TICS minc | | .ds | | | | | |
| 40 | | | (xi) | | | | | lin PTIO | | EQ I | D NO | : 17 | 3: | | | |
| | Met 1 | | . Xaa | His | Phe 5 | Leu | Leu | Val | Ala | Leu 10 | | Ser | Val | Pro | His 15 | Cys |
| 45 | Pro | His | Leu | Leu 20 | | Glu | Glu | His | Lys 25 | Leu | Cys | Lys | Val | Ser 30 | His | Phe |
| 50 | Ser | Gly | Val 35 | | Leu | Val | Thr | Ser 40 | | Gln | Asp | Ser | Ser 45 | Ser | Tyr | Val |
| 50 | Pro | Val 50 | | Thr | Leu | Phe | Ile 55 | | Leu | Gly | Pro | Trp 60 | | Trp | Asp | Leu |
| 55 | Xaa 65 | | Cys | Thr | Ala | Glu 70 | | Pro | Glu | Ala | Glu 75 | | Ser | Leu | Arg | Leu 80 |
| | Cys | His | s Ser | His | Leu 85 | | Arg | Xaa | Asn | Val | | Pro | Ser | Gln | Ala 95 | Ala |
| 60 | Glu | Gly | y Xaa | xaa | Xaa | Arg | Gly | Cys | Gln | His | Arg | Gly | ser, | Arg | Glu | Leu |

| | | | | 100 | | | | | 105 | | | | | 110 | | |
|-----|-----------|-----------|------------|------------|-------------------------|-----------------------|---------------------|-------------------------|--------------------|-----------|-----------|-----------|------------|------------|-----------|-----------|
| 5 | Thr | Phe | Leu 115 | Ser | Ala | Glu | Asn | Glu 120 | Ala | Gly | Ile | | | | | |
| | (2) | INFO | CAMAC | NOIT | FOR | SEQ | ID N | 10: 1 | 74: | | | | | | | |
| 10 | | | (i) : | (. | A) L | ENGTI | H: 1 | ERIST 29 ar no ac | nino | | is | | | | | |
| 1.5 | | | (xi) | | | | | line TION | | EQ II | NO: | : 174 | 1: | | | |
| 15 | Met 1 | Lys | Val | Gly | Ala 5 | Arg | Ile | Arg | Val | Lys 10 | Met | Ser | Val | Asn | Lys 15 | Ala |
| 20 | His | Pro | Val | Val 20 | Ser | Thr | His | Trp | Arg 25 | Trp | Pro | Ala | Glu | Trp 30 | Pro | Gln |
| | Met | Phe | Leu 35 | His | Leu | Ala | Gln | Glu 40 | Pro | Arg | Thr | Glu | Val 45 | Lys | Ser | Arg |
| 25 | Pro | Leu 50 | Gly | Leu | Ala | Gly | Phe 55 | Ile | Arg | Gln | Asp | Ser 60 | Lys | Thr | Arg | Lys |
| • | Pro 65 | Leu | Glu | Gln | Glu | Thr 70 | Ile | Met | Ser | Ala | Ala 75 | Asp | Thr | Ala | Leu | Trp 80 |
| 30 | Pro | Туг | Gly | His | Gly 85 | Asn | Arg | Glu | His | Gln 90 | Glu | Asn | Glu | Leu | Gln 95 | Lys |
| 35 | Tyr | Leu | Gln | Туг 100 | Lys | Asp | Met | His | Leu 105 | Leu | Asp | Ser | Gly | Gln 110 | Ser | Leu |
| | Gly | His | Thr 115 | His | Thr | Leu | Gln | Gly 120 | Ser | His | Asn | Leu | Thr 125 | Ala | Leu | Asn |
| 40 | Ile | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| 45 | (2) | INF | | | | | | NO: | | ٠. | | | | | | |
| 50 | | | | (| (A) I (B) I (D) I | ENGT YPE : OPOL | H: 3 ami OGY: | 72 a no a lin | mino cid ear | aci | | : 17 | 5: | | | |
| | Met | | Tyr | His | Ser 5 | | Leu | Val | Glu | Pro | Ile | Ser | Cys | His | Ala 15 | Trp |
| 55 | Asn | Lys | : Asp | Arg 20 | | Gln | Ile | Ala | Ile 25 | | Pro | Asn | Asn | His | Glu | Val |
| 60 | His | : Ile | тут 35 | | Lys | Ser | Gly | Ala | | Trp | Thr | Lys | Val 45 | | Glu | Leu |

| | Lys | Glu 50 | His | Asn | Gly | Gln | Val 55 | Thr | Gly | Ile | Asp | Trp 60 | Ala | Pro | Glu | Ser |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|--------------------|
| 5 | Asn 65 | Arg | Ile | Val | Thr | Cys 70 | Gly | Thr | Asp | Arg | Asn 75 | Ala | Tyr | Val | Trp | Thr 80 |
| 10 | Leu | Lys | Gly | Arg | Thr 85 | Trp | Lys | Pro | Thr | Leu 90 | Val | Ile | Leu | Arg | Ile 95 | Asn |
| 10 | Arg | Ala | Ala | Arg 100 | Cys | Val | Arg | Trp | Ala 105 | Pro | Asn | Glu | Asn | Lys 110 | Phe | Ala |
| 15 | Val | Gly | Ser 115 | Gly | Ser | Arg | Val | 11e 120 | Ser | Ile | Cys | Tyr | Phe 125 | Glu | Gln | Glu |
| | Asn | Asp 130 | Trp | ·Trp | Val | Cys | Lys 135 | His | Ile | Lys | Lys | Pro 140 | Ile | Arg | Ser | Thr |
| 20 | Val 145 | Leu | Ser | Leu | Asp | Trp 150 | His | Pro | Asn | Asn | Val 155 | Leu | Leu | Ala | Ala | Gly 1 60 |
| 25 | Ser | Cys | Asp | Phe | Lys 165 | Cys | Arg | Ile | Phe | Ser 170 | Ala | Tyr | Ile | Lys | Glu 175 | Val |
| | Glu | Glu | Arg | Pro 180 | Ala | Pro | Thr | Pro | Trp 185 | Gly | Ser | Lys | Met | Pro 190 | Phe | Gly |
| 30 | Glu | Leu | Met 195 | Phe | Glu | Ser | Ser | Ser 200 | Ser | Cys | Gly | Trp | Val 205 | His | Gly | Val |
| | Cys | Phe 210 | Ser | Ala | Ser | Gly | Ser 215 | Arg | Val | Ala | Trp | Val 220 | Ser | His | Asp | Ser |
| 35 | Thr 225 | Val | Cys | Leu | Ala | Asp 230 | Ala | Asp | Lys | Lys | Met 235 | Ala | Val | Ala | Thr | Leu 240 |
| 40 | Ala | Ser | Glu | Thr | Leu 245 | Pro | Leu | Leu | Ala | Leu 250 | Thr | Phe | Ile | Thr | Asp 255 | Asn |
| | Ser | Leu | Val | Ala 260 | Ala | Gly | His | Asp | Cys 265 | Phe | Pro | Val | Leu | Phe 270 | Thr | Tyr |
| 45 | Asp | Ala | Ala 275 | Ala | Gly | Met | Leu | Ser 280 | Phe | Gly | Gly | Arg | Leu 285 | Asp | Val | Pro |
| | Lys | Gln 290 | | Ser | Gln | Arg | Gly 295 | Leu | Thr | Ala | Arg | G1u 300 | | Phe | Gln | Asn |
| 50 | Leu 305 | | Lys | Lys | Ala | Ser 310 | | Glu | Gly | Gly | Thr 315 | | Ala | Gly | Ala | Gly 320 |
| 55 | Leu | Asp | Ser | Leu | His 325 | _ | Asn | Ser | Val | Ser 330 | | Ile | Ser | Val | Leu 335 | |
| | Gly | Gly | Lys | Ala 340 | _ | Cys | Ser | Gln | Phe 345 | _ | Thr | Thr | Gly | Met 350 | Asp | Gly |
| 60 | Gly | Met | Ser 355 | | Trp | Asp | Val | Lys 360 | | Leu | Glu | Ser | Ala 365 | Leu | Lys | Asp |

Leu Lys Ile Lys 370

5

(2) INFORMATION FOR SEQ ID NO: 176:

(i) SEQUENCE CHARACTERISTICS:

10

- (A) LENGTH: 216 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 176:

Met Trp Ser Ile Gly Ala Gly Ala Leu Gly Ala Ala Ala Leu Ala Leu 1 5 10 15

20

Leu Glu Tyr Leu Glu Asp Ile Asp Leu Lys Thr Leu Glu Lys Glu Pro 35 40 45

Arg Thr Phe Lys Ala Lys Glu Leu Trp Glu Lys Asn Gly Ala Val Ile 25 50 55 60

Met Ala Val Arg Arg Pro Gly Cys Phe Leu Cys Arg Glu Glu Ala Ala 65 70 75 80

Asp Leu Ser Ser Leu Lys Ser Met Leu Asp Gln Leu Gly Val Pro Leu 85 90 95

Tyr Ala Val Val Lys Glu His Ile Arg Thr Glu Val Lys Asp Phe Gln 100 105 110

35

Pro Tyr Phe Lys Gly Glu Ile Phe Leu Asp Glu Lys Lys Lys Phe Tyr 115 120 125

Gly Pro Gln Arg Arg Lys Met Met Phe Met Gly Phe Ile Arg Leu Gly 40 130 135 140

45 Leu Glu Gly Glu Gly Phe Ile Leu Gly Gly Val Phe Val Val Gly Ser 165 170 175

Gly Lys Gln Gly Ile Leu Leu Glu His Arg Glu Lys Glu Phe Gly Asp 180 185 190

50

Lys Val Asn Leu Leu Ser Val Leu Glu Ala Ala Lys Met Ile Lys Pro 195 200 205

(2) INFORMATION FOR SEQ ID NO: 177:

| | | | | (1 | ENCE A) Li B) T D) T | ENGTI YPE : OPOLO | H: 5! amir DGY: | 5 am: no ac line | ino a cid ear | | | | | | | |
|----|-----------|-----------|----------------|-------------|--------------------------------------|-------------------------|-----------------------|-------------------------|-----------------------|-----------|-------|-----------|-----------|-----------|-----------|-----------|
| 5 | | | (xi) | SEQU | JENCI | E DES | SCRIE | 1OITS | 1: SE | EQ II | NO: | 177 | : | | | |
| | Met 1 | Lys | Pro | Val | Ser 5 | Arg | Arg | Thr | Leu | Asp 10 | Trp | Ile | Tyr | Ser | Val 15 | Leu |
| 10 | Leu | Leu | Ala | 11e 20 | Val | Leu | Ile | Ser | Trp 25 | Gly | Cys | Ile | Ile | Tyr 30 | Ala | Ser |
| 15 | Met | Val | Ser 35 | Ala | Arg | Arg | Gln | Leu 40 | Arg | Lys | Lys | Tyr | Pro 45 | Asp | Lys | Ile |
| 13 | Phe | Gly 50 | Thr | Asn | Glu | Asn | Leu 55 | | | • | | | | | | |
| 20 | (2) | INF | OR MA ' | TION | FOR | SEQ | ID 1 | NO: I | 178: | | | | | | | |
| 25 | | | | ((| ENCE A) L B) T D) T UENC | ENGT YPE: OPOL | H: 2 ami OGY: | 3 am no a lin | ino cid ear | acid | | : 178 | 3: | | | |
| 30 | Met 1 | Ala | Ala | Asn | Thr 5 | Phe | Val | Leu | Ile | Met 10 | Gly | Ile | Pro | Thr | Ser 15 | Ala |
| 35 | Asn | Ala | Xaa | Arg 20 | Asp | Leu | Phe | | | | | | | | | |
| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 179: | | | | | | | |
| 40 | | | | | JENCE (A) I (B) I (D) I | ENGT TYPE : TOPOI | TH: 1 ami OGY: | l03 ā ino ā : lir | amino acid near | aci | | : 17 | 9: | | | |
| 45 | Met 1 | | : Ile | e Cys | His 5 | | Gly | Thr | Gly | lle 10 | | Leu | Ser | Ala | Gly 15 | Val |
| 50 | Ser | Leu | ı Phe | e Gly 20 | | . Ser | Ala | Leu | Leu 25 | | Pro | Gly | Asn | Phe 30 | | Ser |
| 50 | Tyr | Leu | ı Glı 39 | | ı Val | Lys | s Ser | Leu 40 | | Leu | Gly | Pro | Ala 45 | | Ile | His |
| 55 | Thr | : Ala | | s Phe | e Ala | a Lev | ı Val | | e Pro | Leu | Met | Туr 60 | | Thr | Trp | Asn |
| | Gly 65 | | e Ar | g His | s Lei | Met 70 | | as C |) Lev | ı Gly | / Lys | | Leu | Lys | s Il∈ | Pro 80 |
| 60 | Glr | ı Lei | и Ту | r Gl | n Sei | r Gly | y Vai | l Vai | l Va | l Le | ı Val | Leu | Thr | · Val | l Leι | ı Ser |

304

| | | | | | 85 | | | | | 90 | | | | | 95 | |
|----|-----------|-----------|---------------|----------------|-----------------------|-----------------------|-----------------------|---------------------|---------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 5 | Ser | Met | Gly | Leu 100 | Ala | Ala | Met | | | | | | | | | |
| | (2) | INFO | ORMAT | NOI | FOR | SEQ | ID N | 10: 1 | 180: | | | | | | | |
| 10 | | | (i) : (xi) | (; (; (; | A) L: B) T D) T | ENGT YPE : OPOL | H: 4: amin OGY: | 8 am no a lin | ino a cid ear | acid | | · 18 | n - | | | |
| 15 | | | Lys | | | | | | | | | | | Cys | Gln 15 | Ile |
| 20 | 1 Ser | Gly | Thr | Val 20 | | Phe | Phe | Leu | Phe 25 | | Phe | Ser | Cys | Phe 30 | | Met |
| | Gln | Ala | Gln 35 | Cys | Asp | Lys | Phe | Val 40 | Gly | Trp | Asp | Phe | Phe 45 | Phe | Phe | Leu |
| 25 | | | | | | | | | | | | | | | | |
| 30 | (2) | INF | ORMA' | | | | | | l81: FICS | : | | | | | | |
| 35 | | | (xi) | (| в) т D) т | YPE: OPOL | ami OGY: | no a lin | | | | : 18 | 1: | | | |
| 40 | Met 1 | Arg | Arg | Ala | Leu 5 | Ile | Pro | Pro | Cys | Arg 10 | Gly | Gly | Pro | Ser | Ala 15 | Ser |
| 40 | Asp | Xaa | Cys | Cys 20 | Ser | Cys | Ser | Pro | Ser 25 | Gly | Phe | Ser | Ala | Gly 30 | Arg | Gly |
| 45 | Arg | Cys | Pro 35 | Val | Gln | Gly | Cys | Leu 40 | Arg | Pro | His | Arg | Val 45 | Gln | Leu | Leu |
| | Arg | Arg 50 | Trp | Gly | Pro | Gly | Ser 55 | Pro | Ala | Gly | Gln | Arg 60 | Leu | Ser | Lys | Gly |
| 50 | Phe 65 | | Leu | Leu | Arg | Trp 70 | Trp | Gly | Pro | Gly | Ser 75 | Pro | Ala | Pro | Glu | Pro 80 |
| 55 | Arg | Lys | Gly | Pro | Phe 85 | Pro | Pro | Pro | Asp | Pro 90 | Pro | Trp | Pro | Val | Thr 95 | Leu |

BNSDOCID: <WO__9842738A1_IA>

| | (2) | INF | ORMA! | rion | FOR | SEQ | ID N | 10: 1 | 182: | | | | | | | |
|----|-----------|-----------|-----------|------------|-------------------------|-----------------------|-------------------------|-------------------------|-----------|-----------|-----------|---------------|-----------|-----------|-----------|-----------|
| 5 | | | | ~ (. () | A) L B) T D) T | ENGT YPE : OPOL | H: 9 ami: OGY: | 5 am no a lin | | acid | | : 18 | 2: | | | |
| 10 | Met 1 | Leu | Glu | Thr | Thr 5 | Lys | His | Val | Gln | Ile 10 | Ala | Cys | Met | Leu | Leu 15 | Leu |
| | Thr | Cys | Gln | Ile 20 | Phe | Leu | Pro | Ser | Ser 25 | Leu | Ser | Pro | Ser | Phe 30 | Ile | His |
| 15 | Ser | Leu | Thr 35 | Asp | Ser | Phe | Ile | Pro 40 | Leu | Lys | Lys | Leu | Тут 45 | Val | Cys | Phe |
| 20 | Val | Gln 50 | | Thr | Leu | Leu | Lys 55 | Ala | Ala | Gly | Tyr | Lys 60 | Ser | Ile | Ser | Glu |
| | Ala 65 | Leu | Gly | Phe | Asp | Xaa 70 | Leu | Leu | Cys | Ser | Ser 75 | Ala | Arg | Phe | Val | Trp 80 |
| 25 | Ile | Cys | His | Thr | Tyr 85 | Ser | Arg | Pro | Leu | Val 90 | Thr | Cys | Ala | Leu | His 95 | |
| 30 | (2) | INF | ORMA | TION | FOR | SEQ | ID 1 | NO: | 183: | | | | | | | |
| | | | (i) | - (| A) L B) I | | H: 2 ami | 7 am no a | | | ls | | | | | |
| 35 | | | (xi) | | | | | | N:S | EQ I | D NO | : 18 | 3: | | | |
| | Met 1 | | Val | Ile | Gly 5 | Gly | Leu | Leu | Leu | Val 10 | Val | Ala | Leu | Gly | Pro 15 | Gly |
| 40 | Gly | Val | Ser | Met 20 | _ | Glu | Lys | Lys | Lys 25 | Glu | Trp | | | | | |
| 45 | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 184: | | | | | | | |
| 50 | | | | (| (A) I (B) I (D) I | ENGT TYPE : | TH: 1 : ami LOGY: | il an ino a : lir | | ació | |): 1 8 | 34: | | | |
| | Met | | Gly | , Gly | Leu 5 | | Phe | . Leu | Leu | Leu 10 | | | | | | |
| 55 | 1 | | | | J | | | | | 10 | | | | | | |
| | (2) | INF | FORMA | MOITA | FOR | SEÇ | D | NO: | 185: | | | | | | | |
| 60 | | | / ÷ \ | CEOI | TENICE | CHI | ים א כיו | прото | em r c c | ٠. | | | | | | |

306

(A) LENGTH: 65 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 185: 5 Met Phe Ala Asp Phe Ile Val Val Thr Ala Thr Val Gln Arg Cys Pro 10 Gly Ser Pro Pro Leu Ser Glu Ile Leu Trp Lys Asp Glu Pro Phe Ala 10 25 20 Ile Ser Ser His Ala Gly Leu Pro Trp Leu Ser Ser Trp Pro Ala Pro 40 15 Pro Trp Thr Trp Ser Trp Ile Ser Arg Arg Glu His Gly Arg Gly Ser 65 20 (2) INFORMATION FOR SEQ ID NO: 186: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 186: 30 Met Val Glu Ser Val Met Pro Val Val Val Cys Thr Leu Ser Pro Gly Ile Asp Ser Ser Pro Ser 35 20 (2) INFORMATION FOR SEQ ID NO: 187: 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 132 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 187: Met Asp Val Leu Phe Val Ala Ile Phe Ala Val Pro Leu Ile Leu Gly 50 Gln Glu Tyr Glu Asp Glu Glu Arg Leu Gly Glu Asp Glu Tyr Tyr Gln 25 30 Val Val Tyr Tyr Tyr Thr Val Thr Pro Ser Tyr Asp Asp Phe Ser Ala 55 Asp Phe Thr Ile Asp Tyr Ser Ile Phe Glu Ser Glu Asp Arg Leu Asn 55 60 Arg Leu Asp Lys Asp Ile Thr Glu Ala Ile Glu Thr Thr Ile Ser Leu 60 75 65 70

| | Glu | Thr | Ala | Arg | Ala 85 | Asp | His | Pro | Lys | Pro 90 | Val | Thr | Val | Lys | Pro 95 | Val |
|----|-----------|------------|------------|------------|-------------------------|-----------------------|-------------------------------------|-------------------------|----------------------|-----------|-----|-----------|-------------|------------|-----------|-----|
| 5 | Thr | Thr | Glu | Pro 100 | Gln | Ser | Pro | Asp | Leu 105 | Asn | Asp | Ala | Val | Ser 110 | Ser | Leu |
| 10 | Arg | Ser | Pro 115 | Ile | Pro | Leu | Leu | Leu 120 | Ser | Cys | Ala | Phe | Val 125 | Gln | Val | Gly |
| 10 | Met | Туг 130 | Phe | Met | | | | | | | | | | | | |
| 15 | (2) | INF | ORMA' | rion | FOR | SEQ | ID I | NO: 1 | 188: | | | | | | | |
| 20 | | | | ~ (| A) L B) T D) T | ENGT YPE : OPOL | RACT H: 6 ami OGY: SCRI | 9 am no a lin | ino cid ear | acid | | : 18 | 8: | | | |
| 25 | Met 1 | Pro | Cys | Gln | Pro 5 | Gly | Gln | Val | Pro | Ser 10 | Cys | Gln | Cys | Thr | Phe 15 | Gly |
| | Leu | Leu | Leu | Met 20 | Leu | Pro | Ser | Leu | Pro 25 | Ser | Pro | Ala | Ser | Gln 30 | Pro | Arg |
| 30 | Pro | Phe | Cys 35 | Ser | Ser | Met | Glu | Tyr 40 | Phe | His | Gly | Cys | Ala 45 | Ser | Pro | Ser |
| 35 | Gln | Ala 50 | Ile | Ile | Gly | Gly | Phe 55 | Pro | Phe | Ala | Ser | Val 60 | Ala | Leu | Ala | Asp |
| 55 | Ile 65 | Leu | Cys | Leu | Gln | | | | | | | | | | | |
| 40 | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 189: | | | | | | | |
| 45 | | | | | (A) I (B) I (D) I | ENGT YPE : OPOI | RACT TH: 4 : ami LOGY: | l5 an ino a : lir | mino acid near | acid | |): 18 | 19 : | | | |
| 50 | Met | | | - | •' | Pro | | | | | Leu | | | Ile | Phe 15 | |
| | Leu | . Met | . Phe | Phe 20 | | Phe | Pro | Phe | Arg 25 | | His | Thr | · Val | Val | | Ile |
| 55 | Val | . Ala | Ser 35 | _ | Phe | . Leu | Gly | Leu 40 | | Pro | Leu | ı Cys | Gly 45 | | | |
| 60 | (2) | INF | FORM | 4OITA | I FOF | SEC |) ID | NO: | 190: | | | | | | | |

| 5 | | | (i) s (xi) | (| A) L B) T D) T | ENGTI YPE : OPOL | H: 69 amin DGY: | 5 am no a line | ino a cid ear | acid: | | : 190 |): | | | |
|----|-----------|------------------|---------------|-----------|-------------------------|---|------------------------|---------------------------------|--------------------------------|-----------|-------|-----------|-----------|-----------|-----------|-----|
| 10 | Met 1 | Ala | Phe | Gly | Leu 5 | Gln | Met | Phe | Ile | Gln 10 | Arg | Lys | Phe | Pro | Туг 15 | Pro |
| 10 | Leu | Gln | Trp | Ser 20 | Leu | Leu | Val | Ala | Val 25 | Val | Ala | Gly | Ser | Val 30 | Val | Ser |
| 15 | Tyr | Gly | Val 35 | Thr | Arg | Val | Glu | Ser 40 | Glu | Lys | Cys | Asn | Asn 45 | Leu | Trp | Leu |
| | Phe | Leu 50 | Glu | Thr | Gly | Gln | Leu 55 | Pro | Lys | Asp | Arg | Ser 60 | Thr | Asp | Gln | Arg |
| 20 | Ser 65 | | | | | | | | | | | | | | | |
| 25 | (2) | INF | ORMA' | TION | FOR | SEQ | ID 1 | 1 10: [| 191: | | | | | | | |
| 30 | | | | ((| A) L B) T D) T | CHA ENGT YPE: YOPOL E DE | H: 5 ami OGY: | 0 am no a lin | ino cid ear | acid | | : 19 | 1: | | | |
| 35 | Met | Asn | Leu | Leu | Gly 5 | | Ile | Phe | Ser | Met 10 | Cys | Gly | Leu | Met | Leu 15 | Lys |
| 33 | Leu | Lys | Trp | Cys 20 | | Trp | Val | Ala | Val 25 | Tyr | Cys | Ser | Phe | Ile 30 | Ser | Phe |
| 40 | Ala | Asn | Ser 35 | | Ser | Ser | Glu | Asp 40 | | Lys | Gln | Met | Met 45 | Ser | Ser | Phe |
| | Met | Xaa 50 | | | | | | | | | | | | | | |
| 45 | (2) | TNE | ORMA | MOTT. | ı FOR | SEO | ID | NO: | 192: | | | | | | | |
| 50 | ν, | | (i) | SEQU | JENCI (A) 1 (B) ' | E CHA LENGT LYPE L'OPOI CE DE | RACT TH: 1 : ami | ERIS 170 a ino a : lir | STICS amino acid near | ac: | | D: 19 | 92: | | | |
| 55 | Met | | ı Lev | ı Asr | ı Val | | Leu | Val | . Ala | Leu 10 | | . Leu | ı Leu | Gly | Ala 15 | |
| 60 | Arg | ı Leı | ı Trp | 20 | | Trp | Gly | Arg | Arg 25 | | / Leu | ı Gly | Ala | Gly 30 | | Gly |

| | Ala | Gly | Glu 35 | Glu | Ser | Pro | Ala | Thr 40 | Ser | Leu | Pro | Arg | Met 45 | Lys | Lys | Arg |
|----|------------|------------|-------------|------------|-------------------------|---------------------------------------|---------------------|----------------------|----------------------|------------|------------|---------------|------------|------------|-----------|------------|
| 5 | Asp | Phe 50 | Ser | Leu | Glu | Gln | Leu 55 | Arg | Gln | Tyr | Asp | Gly 60 | Ser | Arg | Asn | Pro |
| | Arg 65 | Ile | Leu | Leu | Ala | Val 70 | Asn | Gly | Lys | Val | Phe 75 | Asp | Val | Thr | Lys | Gly 80 |
| 10 | Ser | Lys | Phe | Tyr | Gly 85 | Pro | Ala | Gly | Pro | Туг 90 | Gly | Ile | Phe | Ala | Gly 95 | Arg |
| 15 | Asp | Ala | Ser | Arg 100 | Gly | Leu | Ala | Thr | Phe 105 | Cys | Leu | Asp | Lys | Asp 110 | Ala | Leu |
| | Arg | Asp | Glu 115 | Tyr | Asp | Asp | Leu | Ser 120 | Asp | Leu | Asn | Ala | Val 125 | Gln | Met | Glu |
| 20 | Ser | Val 130 | Arg | Glu | Trp | Glu | Met 135 | Gln | Phe | Lys | Glu | Lys 140 | Tyr | Asp | Tyr | Val |
| | Gly 145 | Arg | Leu | Leu | Lys | Pro 150 | Gly | Glu | Glu | Pro | Ser 155 | Glu | Tyr | Thr | Asp | Glu 160 |
| 25 | Glu | Asp | Thr | Lys | Asp 165 | His | Asn | Lys | Gln | Asp 170 | | | | | | |
| 30 | (2) | INF | | TION | | | | | | | | | | | | |
| 35 | | | (i) (xi) | (| (A) I (B) I (D) I | ENGT YPE: YPE: YOPOL E DE | H: 6 ami OGY: | 66 am no a lir | nino ncid near | ació | |): 1 9 | 3: | | | |
| 40 | Met 1 | | Туг | Phe | Ser 5 | | Leu | Leu | Val | Ile 10 | | Ala | . Phe | Ala | Ala 15 | Trp |
| 40 | Val | Ala | Leu | Ala 20 | | Gly | Leu | Gly | Val 25 | | Val | Туг | Ala | Ala 30 | | Val |
| 45 | Leu | . Leu | Gly 35 | | Gly | Cys | Ala | Thr 40 | | Leu | Val | Thr | Ser 45 | | Ala | Met |
| | Thr | Ala 50 | | Leu | ılle | e Gly | Pro | | Thr | Asr | ser | Gly 60 | | Ser | . Cys | Thr |
| 50 | Ala 65 | Pro | • | | | | | | | | | | | | | |
| 55 | (2) | INE | FORM | 1OITA | 1 FOF | R SEÇ |) ID | NO: | 194: | | | | | | | |
| | | | (i) | SEQ | (A) | E CHA LENG TYPE | TH: | 92 aı | mino | | ds | | | | | |
| 60 | | | | | | TOPO | | | | | | | | | | |

| | | | (xı) | SEQ | UENC | E DE | SCRI | PTIO | N: SI | EQ II | ON C | : 194 | 4: | | | |
|----------|------------|-----------|------------|---------------|--------------|---------------|-------------|------------------------------|-------------|-----------|------------|-----------|------------|-----------|-------------|------------|
| 5 | Met 1 | Ala | Ala | Gly | Pro 5 | Ser | Gly | Cys | Leu | Val 10 | Pro | Ala | Phe | Gly | Leu 15 | Arg |
| 3 | Leu | Leu | Leu | Ala 20 | Thr | Val | Leu | Gln | Ala 25 | Val | Ser | Ala | Phe | Gly 30 | Ala | Glu |
| 10 | Phe | Ser | Ser 35 | Glu | Ala | Cys | Arg | Glu 40 | Leu | Gly | Phe | Ser | Ser 45 | Asn | Leu | Leu |
| | Cys | Ser 50 | Ser | Суѕ | Asp | Leu | Leu 55 | Gly | Gln | Phe | Asn | Leu 60 | Leu | Gln | Leu | Asp |
| 15 | Pro 65 | Asp | Cys | Arg | Gly | Cys 70 | Cys | Gln | Glu | Glu | Ala 75 | Gln | Phe | Glu | Thr | Lys 80 |
| 20 | Lys | Leu | Tyr | Ala | Gly 85 | Ala | Ile | Leu | Glu | Val 90 | Cys | Gly | | | | |
| | (2) | INF | ORMA' | rion | FOR | SEQ | ID 1 | 1 0: 1 | 195: | | | | | | | |
| 25 | | | (i) : | (| A) L B) T | ENGT YPE : | H: 1 ami | ERIS' 76 a no a lin | mino cid | | ds | | | | | |
| 30 | | • | | | | | | PTIO | | | | | | 23- | 3 1- | • |
| | мес 1 | Arg | GTĀ | ser | H1S | ьeu | Arg | Leu | Leu | 10 | туr | Leu | vai | Ala | 15 | Asn |
| 35 | Pro | Val | Asn | Tyr 20 | Gly | Arg | Pro | Tyr | Arg 25 | Leu | Ser | Cys | Val | Glu 30 | Ala | Phe |
| | Ala | Ala | Thr 35 | Phe | Cys | Ile | Val | Gly 40 | Phe | Pro | Asp | Leu | Ala 45 | Val | Ile | Leu |
| 40 | | 50 | | | | | 55 | Lys | | | | 60 | | | | |
| 45 | 65 | | | _ | _ | 70 | | Суѕ | _ | | 75 | | | | | 80 |
| | | | | | 85 | | | Asn | | 90 | | | | | 95 | |
| 50 | | | - | 100 | | | | Asp | 105 | - | J | | | 110 | | |
| . | Asn | Arg | Pro 115 | Val | Ala | Ser | Thr | Arg 120 | Leu | Pro | Ser | Asp | Thr 125 | Asp | Asp | Ser |
| 55 | | 130 | | | | | 135 | Pro | | | | 140 | | | | |
| 60 | Ser 145 | Ser | Cys | Cys | Glu | Glu 150 | Glu | Gln | Thr | Gln | Gly 155 | Arg | Gly | Ala | Glu | Ala 160 |

| | 165 170 175 175 176 Arg Arg Gin Arg Asp | 1 |
|----|---|---|
| .5 | | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 196: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 70 amino acids (B) TYPE: amino acid | |
| 15 | (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196: | |
| | Met Ser Asn Ala Cys Lys Glu Leu Ala Ile Phe Leu Thr Thr Gly Ile 1 5 10 15 | ž |
| 20 | Val Val Ser Ala Phe Gly Leu Pro Ile Val Phe Ala Arg Ala His Leu 20 25 30 | 1 |
| 25 | Ile Glu Trp Gly Ala Cys Ala Leu Val Leu Thr Gly Asn Thr Val Ile 35 40 45 | è |
| 23 | Phe Ala Thr Ile Leu Gly Phe Phe Leu Val Phe Gly Ser Asn Asp Asp 50 55 60 |) |
| 30 | Phe Ser Trp Gln Gln Trp 65 70 | |
| 35 | (2) INFORMATION FOR SEQ ID NO: 197: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear | |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197: Met Thr Leu Leu Ile Ile Phe Leu Pro Phe Xaa Phe Thr Thr Xaa Thr | r |
| 45 | 1 5 10 15 Asn Ser Gly Gly Ser Phe Pro Val Arg 20 25 | |
| 50 | (2) INFORMATION FOR SEQ ID NO: 198: | |
| 55 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 73 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198: | |
| 60 | Met Lys Gly Glu Leu Leu Pro Phe Leu Phe Leu Thr Val Trp Leu Tr 1 5 10 15 | р |

| | Leu | Tyr | Lys | Leu 20 | Xaa | Phe | Gly | Glu | Ser 25 | Pro | Arg | Tyr | Pro | Asn 30 | Val | Ile |
|----|------------|------------|------------|-------------|----------------------|-----------------------|---------------------|---------------------------------------|--------------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Gly | Lys | Thr 35 | Tyr | Phe | Phe | Phe | Trp 40 | Thr | Asp | Gln | Ile | Ser 45 | Arg | Glu | Ser |
| | Arg | Phe 50 | Leu | Glu | Arg | Leu | Ala 55 | Phe | Ile | Val | Ser | Glu 60 | Asn | Cys | Leu | Ile |
| 10 | Phe 65 | Leu | Ile | His | Ala | Ile 70 | Thr | Gly | Gln | | | | | | | |
| 15 | (2) | | | | | | | NO: 1 | | | | | | | | |
| 20 | | | | ~ ((| A) L B) T D) T | ENGT YPE : OPOL | H: 2 ami OGY: | ERIST 89 ai no a lin PTIO | mino cid ear | aci | | : 19 | 9 : | | | |
| 25 | Met 1 | Ser | Gly | Phe | Ser 5 | Thr | Glu | Glu | Arg | Ala 10 | Ala | Pro | Phe | Ser | Leu 15 | Glu |
| 23 | Tyr | Arg | Val | Phe 20 | Leu | Lys | Asn | Glu | Lys 25 | Gly | Gln | Tyr | Ile | Ser 30 | Pro | Phe |
| 30 | His | Asp | Ile 35 | Pro | Ile | Tyr | Ala | Asp 40 | Lys | Asp | Val | Phe | His 45 | Met | Val | Val |
| | Glu | Val 50 | Pro | Arg | Trp | Ser | Asn 55 | Ala | Lys | Met | Glu | Ile 60 | Ala | Thr | Lys | Asp |
| 35 | Pro 65 | Leu | Asn | Pro | Ile | Lys 70 | Gln | Asp | Val | Lys | Lys 75 | Gly | Lys | Leu | Arg | Tyr 80 |
| 40 | Val | Ala | Asn | Leu | Phe 85 | Pro | Tyr | Lys | Gly | Tyr 90 | Ile | Trp | Asn | Tyr | Gly 95 | Ala |
| 70 | Ile | Pro | Gln | Thr 100 | Trp | Glu | Asp | Pro | Gly 105 | His | Asn | Asp | Lys | His 110 | Thr | Gly |
| 45 | Cys | Cys | Gly 115 | Asp | Asn | Asp | Pro | 11e 120 | Asp | Val | Cys | Glu | Ile 125 | Gly | Ser | Lys |
| | Val | Cys 130 | | Arg | Gly | Glu | Ile 135 | Ile | Gly | Val | Lys | Val 140 | | Gly | Ile | Leu |
| 50 | Ala 145 | | Ile | Asp | Glu | Gly 150 | | Thr | Asp | Trp | Lys 155 | | Ile | Ala | Ile | Asn 160 |
| 55 | Val | . Asp | Asp | Pro | Asp 165 | | Ala | . Asn | Tyr | Asn 170 | Asp | Ile | Asn | Asp | Val 175 | |
| | Arg | Leu | Lys | Pro 180 | | Tyr | Leu | Glu | Ala 185 | | Val | Asp | Trp | Phe 190 | | Arg |
| 60 | Tyr | Lys | Val | | Asp | Gly | Lys | Pro 200 | | . Asn | Glu | Phe | Ala 205 | | Asn | Ala |

| | Glu | Phe 210 | Lys | Asp | Lys | Asp | Phe 215 | Ala | Ile | Asp | 11e | 11e 220 | rys | ser | inr | HIS |
|----|------------|------------|--------------|------------|----------------------|----------------------|---------------------|---------------------|--------------------|------------|------------------|------------|------------|------------|--------------------|------------|
| 5 | Asp 225 | His | Trp | Lys | Ala | Leu 230 | Val | Thr | Lys | Lys | Thr 235 | Asn | Gly | Lys | Gly | Ile 240 |
| 10 | Ser | Cys | Met | Asn | Thr 245 | Thr | Leu | Ser | Glu | Ser 250 | Pro | Phe | Lys | Cys | As p 255 | Pro |
| 10 | Asp | Ala | Ala | Arg 260 | Ala | Ile | Val | Asp | Ala 265 | Leu | Pro | Pro | Pro | Суs 270 | Glu | Ser |
| 15 | Ala | Cys | Thr 275 | Val | Pro | Thr | Asp | Val 280 | Asp | Lys | Trp | Phe | His 285 | His | Gln | Lys |
| | Asn | | | | | | | | | | | | | | | |
| 20 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMAT | NOIT | FOR | SEQ | ID 1 | 10: 2 | 200: | | | | | | | |
| 25 | | | (i) : | ((| A) L B) T D) T | ENGT YPE: OPOL | H: 6 ami OGY: | 25 a no a lin | mino cid ear | aci | | . 20 | 0. | | | |
| | | | | | | | | | | | D NO | | | | | |
| 30 | Met 1 | | Ile | Pro | Gly 5 | Ser | Leu | Cys | Lys | Lys 10 | Val | Lys | Leu | Ser | Asn 15 | Asn |
| 35 | Ala | Gln | Asn | Trp 20 | | Met | Gln | Arg | Ala 25 | Thr | Asn | Val | Thr | Туr 30 | Gln | Ala |
| 55 | His | His | : Val 35 | Ser | Arg | Asn | Lys | Arg 40 | Gly | Gln | Val | Val | Gly 45 | Thr | Arg | Gly |
| 40 | Gly | Phe 50 | e Arg | Gly | Cys | Thr | Val 55 | Trp | Leu | Thr | Gly | Leu 60 | | Gly | Ala | Gly |
| | Lys 65 | | Thr | Val | Ser | Met 70 | Ala | Leu | Glu | Glu | Tyr 75 | Leu | Val | Суѕ | His | Gly 80 |
| 45 | Ile | e Pro | Cys | Tyr | Thr 85 | | Asp | Gly | Asp | Asn 90 | | Arg | Gln | Gly | Leu 95 | |
| 50 | Lys | s Asr | ı Leu | Gly 100 | | e Ser | Pro | Glu | Asp 105 | | , Glu | Glu | Asn | Val | | Arg |
| 50 | Ile | e Ala | a Glu 115 | | . Ala | Lys | Leu | Phe 120 | | Asp | Ala | Gly | Leu 125 | | . Cys | : Ile |
| 55 | Th | r Sei | r Phe | e Ile | e Ser | Pro | Туг 135 | | Glr | n Asp | Arg | Asr 140 | | Ala | Arg | g Gln |
| | 11 14 | | s Glu | ı Gly | / Ala | a Ser 150 | | ı Pro |) Phe | e Phe | ∋ Glu 155 | | l Phe | val | L Asp | Ala 160 |
| 60 | Pr | o Le | u His | s Val | l Cys | s Glu | ı Glr | ı Arç | g Ası | va. | l Lys | Gly | / Let | а Туз | c Lys | s Lys |

| | | | | | 165 | | | | | 170 | | | | | 175 | |
|----|--------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Ala | Arg | Ala | Gly 180 | Glu | Ile | Lys | Gly | Phe 185 | Thr | Gly | Ile | Asp | Ser 190 | Glu | Tyr |
| .5 | Glu | Lys | Pro 195 | Glu | Ala | Pro | Glu | Leu 200 | Val | Leu | Lys | Thr | Asp 205 | Ser | Cys | Asp |
| 10 | Val | Asn 210 | Asp | Cys | Val | Gln | Gln 215 | Val | Val | Glu | Leu | Leu 220 | Gln | Glu | Arg | Asp |
| | Ile 225 | Val | Pro | Val | Asp | Ala 230 | Ser | Tyr | Glu | Val | Lys 235 | Glu | Leu | Туr | Val | Pro 240 |
| 15 | Glu | Asn | Lys | Leu | His 245 | Leu | Ala | Lys | Thr | Asp 250 | Ala | Glu | Thr | Leu | Pro 255 | Ala |
| 20 | Leu | Lys | Ile | Asn 260 | Lys | Val | Asp | Met | Gln 265 | Trp | Val | Gln | Val | Leu 270 | Ala | Glu |
| | Gly | Trp | Ala 275 | Thr | Pro | Leu | Asn | Gly 280 | Phe | Met | Arg | Glu | Arg 285 | Glu | Tyr | Leu |
| 25 | Gln | Cys 290 | Leu | His | Phe | Asp | Cys 295 | Leu | Leu | Asp | Gly | Gly 300 | Val | Ile | Asn | Leu |
| | Ser 305 | Val | Pro | Ile | Val | Leu 310 | Thr | Ala | Thr | His | Glu 315 | Asp | Lys | Glu | Arg | Leu 320 |
| 30 | Asp | Gly | Cys | Thr | Ala 325 | Phe | Ala | Leu | Met | Tyr 330 | Glu | Gly | Arg | Arg | Val 335 | Ala |
| 35 | Ile | Leu | Arg | Asn 340 | Pro | Glu | Phe | Phe | Glu 345 | His | Arg | Lys | Glu | Glu 350 | Arg | Cys |
| | Ala | Arg | Gln 355 | Trp | Gly | Thr | Thr | Cys 360 | Lys | Asn | His | Pro | Туг 365 | Ile | Lys | Met |
| 40 | Val | Met 370 | Glu | Gln | Gly | Asp | Trp 375 | Leu | Ile | Gly | Gly | Asp 380 | Leu | Gln | Val | Leu |
| | Asp 385 | Arg | Val | Tyr | Trp | Asn 390 | Asp | Gly | Leu | Asp | Gln 395 | Tyr | Arg | Leu | Thr | Pro 400 |
| 45 | Thr | Glu | Leu | Lys | Gln 405 | Lys | Phe | Lys | Asp | Met 410 | | Ala | Asp | Ala | Val 415 | Ph∈ |
| 50 | Ala | Phe | Gln | Leu 420 | _ | Asn | Pro | Val | His 425 | Asn | Gly | His | Ala | Leu 430 | Leu | Met |
| 50 | Gln | Asp | Thr 435 | | Lys | Gln | Leu | Leu 440 | Glu | Arg | Gly | Tyr | Arg 445 | Arg | Pro | Va] |
| 55 | Leu | Leu 450 | | His | Pro | Leu | Gly 455 | _ | Trp | Thr | Lys | Asp 460 | Asp | Asp | Val | Pro |
| | Leu 4 65 | | Trp | Arg | Met | Lys 470 | | His | Ala | Ala | Val 475 | Leu | Glu | Glu | Gly | Va] 480 |
| 60 | Leu | Asn | Pro | Glu | Thr | Thr | Val | Val | Ala | Ile | Phe | Pro | Ser | Pro | Met | Met |

| | | | | | 485 | | | | | 490 | | | | | 495 | |
|----|------------|------------|------------|------------|------------------------------|---------------|-------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Tyr | Ala | Gly | Pro 500 | Thr | Glu | Val | Gln | Trp 505 | His | Cys | Arg | Ala | Arg 510 | Met | Val |
| J | Ala | Gly | Ala 515 | Asn | Phe | Туг | Ile | Val 520 | Gly | Arg | Asp | Pro | Ala 525 | Gly | Met | Pro |
| 10 | His | Pro 530 | Glu | Thr | Gly | Lys | Asp 535 | Leu | Tyr | Glu | Pro | Ser 540 | His | Gly | Ala | Lys |
| | Val 545 | Leu | Thr | Met | Ala | Pro 550 | Gly | Leu | Ile | Thr | Leu 555 | Glu | Ile | Val | Pro | Phe 560 |
| 15 | Arg | Val | Ala | Ala | Туг 565 | Asn | Lys | Lys | Lys | Lys 570 | Arg | Met | Asp | Tyr | Туr 575 | Asp |
| 20 | Ser | Glu | His | His 580 | Glu | Asp | Phe | Glu | Phe 585 | Ile | Ser | Gly | Thr | Arg 590 | Met | Arg |
| | Lys | Leu | Ala 595 | Arg | Glu | Gly | Gln | Lуs 600 | Pro | Pro | Glu | Gly | Phe 605 | Met | Ala | Pro |
| 25 | Lys | Ala 610 | Trp | Thr | Val | Leu | Thr 615 | Glu | Tyr | Tyr | Lys | Ser 620 | Leu | Glu | Lys | Ala |
| | Xaa 625 | | | | | | | | | | | | | | | |
| 30 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA' | rion | FOR | SEQ | ID | NO: | 201: | | | | | | | |
| 35 | | | (i) | (| ENCE A) L B) T D) T | ENGT YPE : | H: 6 ami | 49 a.no a | mino cid | | .ds | | | | | |
| | | | (xi) | | UENC | | | | | EQ I | D NO | : 20 | 1: | | | |
| 40 | Met 1 | Ser | Ala | Ser | Gln 5 | | Leu | Glu | Pro | Lys 10 | Pro | Leu | Phe | Pro | Lys 15 | Pro |
| 45 | Ala | Phe | Gly | Gln 20 | Lys | Pro | Pro | Leu | Ser 25 | Thr | Glu | Asn | Ser | His 30 | Glu | Asp |
| | Glu | Ser | Pro 35 | | Lys | Asn | Val | Ser 40 | | Ser | Lys | Gly | Ser 45 | | Ala | Pro |
| 50 | Leu | Gly 50 | Val | Arg | Ser | Lys | Ser 55 | | Pro | Leu | Lys | Pro 60 | | Arg | Glu | Asr |
| | Ser 65 | | Asn | Lys | Asp | His 70 | | Gly | Glu | lle | Ser 75 | | Leu | Pro | Phe | Pro 80 |
| 55 | Gly | Val | . Val | Leu | Lys 85 | | Ala | Ala | Ser | Arg 90 | | Gly | Pro | Gly | Leu 95 | |
| 60 | Lys | Asn | ı Gly | Glu 100 | | Lys | : Lys | : Glu | Asp 105 | | , Lys | : Ile | e Asp | Ala 110 | | Lys |

| | Asn | Thr | Phe 115 | Gln | Ser | Lys | Ile | Asn 120 | Gln | Glu | Glu | Leu | Ala 125 | Ser | Gly | Thr |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Pro | Pro 130 | Ala | Arg | Phe | Pro | Lys 135 | Ala | Pro | Ser | Lys | Leu 140 | Thr | Val | Gly | Gly |
| | Pro 145 | Trp | Gly | Gln | Ser | Gln 150 | Glu | Lys | Glu | Lys | Gly 155 | Asp | Lys | Asn | Ser | Ala 160 |
| 10 | Thr | Pro | Lys | Gln | Lys 165 | Pro | Leu | Pro | Pro | Leu 170 | Phe | Thr | Leu | Gly | Pro 175 | Pro |
| 15 | Pro | Pro | Lys | Pro 180 | Asn | Arg | Pro | Pro | Asn 185 | Val | Asp | Leu | Thr | Lys 190 | Phe | His |
| 15 | Lys | Thr | Ser 195 | Ser | Gly | Asn | Ser | Thr 200 | Ser | Lys | Gly | Gln | Thr 205 | Ser | Tyr | Ser |
| 20 | Thr | Thr 210 | Ser | Leu | Pro | Pro | Pro 215 | Pro | Pro | Ser | His | Pro 220 | Ala | Ser | Gln | Pro |
| | Pro 225 | Leu | Pro | Ala | Ser | His 230 | Pro | Ser | Gln | Pro | Pro 235 | Val | Pro | Ser | Leu | Pro 240 |
| 25 | Pro | Arg | Asn | Ile | Lys 245 | Pro | Pro | Phe | Asp | Leu 250 | Lys | Ser | Pro | Val | Asn 255 | Glu |
| 30 | Asp | Asn | Gln | Asp 260 | Gly | Val | Thr | His | Ser 265 | Asp | Gly | Ala | Gly | Asn 270 | Leu | Asp |
| 50 | Glu | Glu | Gln 275 | Asp | Ser | Glu | Gly | Glu 280 | Thr | Tyr | Glu | Asp | Ile 285 | Glu | Ala | Ser |
| 35 | Lys | Glu 290 | Arg | Glu | Lys | Lys | Arg 295 | Glu | Lys | Glu | Glu | Lys 300 | Lys | Arg | Leu | Glu |
| | Leu 305 | Glu | Lys | Lys* | Glu | Gln 310 | Lys | Glu | Lys | Glu | Lys 315 | Lys | Glu | Gln | Glu | Ile 320 |
| 40 | Lys | Lys | Lys | Phe | Lys 325 | Leu | Thr | Gly | Pro | Ile 330 | Gln | Val | Ile | His | Leu 335 | Ala |
| 45 | Lys | Ala | Cys | Cys 340 | Asp | Val | Lys | Gly | Gly 345 | Lys | Asn | Glu | Leu | Ser 350 | Phe | Lys |
| 4 5 | Gln | Gly | Glu 355 | Gln | Ile | Glu | Ile | Ile 360 | Arg | Ile | Thr | Asp | Asn 365 | Pro | Glu | Gly |
| 50 | Lys | Trp 370 | Leu | Gly | Arg | Thr | Ala 375 | Arg | Gly | Ser | Tyr | Gly 380 | Tyr | Ile | Lys | Thr |
| | Thr 385 | Ala | Val | Glu | Ile | Asp 390 | Tyr | Asp | Ser | Leu | Lys 395 | Leu | Lys | Lys | Asp | Ser 400 |
| 55 | Leu | Gly | Ala | Pro | Ser 405 | Arg | Pro | Ile | Glu | Asp 410 | Asp | Gln | Glu | Val | Туг 415 | Asp |
| 60 | Asp | Val | Ala | Glu 420 | Gln | Asp | Asp | Ile | Ser 425 | Ser | His | Ser | Gln | Ser 430 | Gly | Ser |

| | Gly | Gly | 11e 435 | Phe | Pro | Pro | Pro | Pro 440 | Asp | Asp | Asp | Ile | Туг 445 | Asp | Gly | Ile |
|----|------------|------------|------------|------------|--------------------------------------|----------------------|---------------------|---------------------|-------------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Glu | Glu 450 | Glu | Asp | Ala | Asp | Asp 455 | Gly | Ser | Thr | Leu | Gln 460 | Val | Gln | Glu | Lys |
| | Ser 465 | Asn | Thr | Trp | Ser | Trp 470 | Gly | Ile | Leu | Lys | Met 475 | Leu | Lys | Gly | Lys | Asp 480 |
| 10 | Asp | Arg | Lys | Lys | Ser 485 | Ile | Arg | Glu | Lys | Pro 490 | Lys | Val | Ser | Asp | Ser 495 | Asp |
| 15 | Asn | Asn | Glu | Gly 500 | Ser | Ser | Phe | Pro | Ala 505 | Pro | Pro | Lys | Gln | Leu 510 | Asp | Met |
| 15 | Gly | Asp | Glu 515 | Val | Tyr | Aşp | Asp | Val 520 | Asp | Thr | Ser | Asp | Phe 525 | Pro | Val | Ser |
| 20 | Ser | Ala 530 | Glu | Met | Ser | Gln | Gly 535 | Thr | Asn | Val | Gly | Lys 540 | Ala | Lys | Thr | Glu |
| | Glu 545 | Lys | Asp | Leu | Lys | Lys 550 | Leu | Lys | Lys | Gln | Xaa 555 | Lys | Xaa | Xaa | Lys | Asp 560 |
| 25 | Phe | Arg | Lys | Lys | Phe 565 | Lys | Tyr | Asp | Gly | Glu 570 | Ile | Arg | Val | Leu | Tyr 575 | Ser |
| 30 | Thr | Lys | Val | Thr 580 | Thr | Ser | Ile | Thr | Ser 585 | Lys | Lys | Trp | Gly | Thr 590 | Arg | Asp |
| 50 | Leu | Gln | Val 595 | Lys | Pro | Gly | Glu | Ser 600 | Leu | Glu | Val | Ile | Gln 605 | Thr | Thr | Asp |
| 35 | Asp | Thr 610 | Lys | Val | Leu | Cys | Arg 615 | Asn | Glu | Glu | Gly | Lys 620 | Tyr | Gly | Tyr | Val |
| | Leu 625 | Arg | Ser | Tyr | Leu | Ala 630 | Asp | Asn | Asp | Gly | Glu 635 | Ile | Tyr | Asp | Asp | I1∈ 640 |
| 40 | Ala | Asp | Gly | Cys | 11e 645 | Tyr | Asp | Asn | Asp | | • | | | | | |
| 45 | (2) | INFO | ORMA' | rion | FOR | SEQ | ID 1 | NO: 2 | 202: | | | | | | | |
| 50 | | | | (| ENCE A) L B) T D) T UENC | ENGT YPE: OPOL | H: 5 ami OGY: | 5 am no a lin | ino cid ear | acid | | : 20 | 2: | | | |
| | Met 1 | Ala | Trp | Pro | Ser 5 | Arg | Ser | Lys | Met | Phe 10 | Thr | Leu | Leu | Pro | Val 15 | Leu |
| 55 | | Туr | Leu | Trp 20 | | Leu | Trp | Leu | Pro 25 | | Phe | Ser | Trp | Ile 30 | | Glu |
| 60 | Leu | Lys | Ala 35 | Va1 | Leu | Arg | Asp | Asp 40 | | Leu | Ile | Ser | Ala 45 | | Ala | Trp |

| | Asn Ala | | Phe | Gln | Thr | Cys 55 | | | | | | | | | |
|----|----------------|--------------|------------|-----------------------|-------------------------|-----------------------|------------------------|--------------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | | | | | | | | | | | | | | | |
| | (2) INF | ORMAT | ION | FOR | SEQ | ID N | 10: 2 | :03: | | | | | | | |
| 10 | | (i) S (xi) | (E | A) L1 B) T O) T | ENGTI YPE : OPOLA | H: 20 amin DGY: | 67 au no ao line | mino cid ear | aci | | : 203 | 3: | | | |
| 15 | Met Val | Lys | Val | Thr 5 | Phe | Asn | Ser | Ala | Leu 10 | Ala | Gln | Lys | Glu | 1 - | Lys |
| 20 | Lys Asp | Glu | Pro 20 | Lys | Ser | Gly | Glu | Glu 25 | Ala | Leu | Ile | Ile | Pro 30 | Pro | Asp |
| 20 | Ala Val | Ala 35 | Val | Asp | Cys | Lys | Asp 40 | Pro | Asp | Asp | Val | Val 45 | Pro | Val | Gly |
| 25 | Gln Arg | | Ala | Trp | Cys | Trp 55 | Cys | Met | Cys | Phe | Gly 60 | Leu | Ala | Phe | Met |
| | Leu Ala 65 | Gly | Val | Ile | Leu 70 | Gly | Gly | Ala | Tyr | Leu 75 | Tyr | Lys | Tyr | Phe | Ala 80 |
| 30 | Leu Glr | Pro | Asp | Asp 85 | Val | Tyr | Tyr | Cys | Gly 90 | Ile | Lys | Tyr | Ile | Lys 95 | Asp |
| 35 | Asp Val | . Ile | Leu 100 | Asn | Glu | Pro | Ser | Ala 105 | Asp | Ala | Pro | Ala | Ala 110 | Leu | Tyr |
| | Gln Thr | 11e 115 | Glu | Glu | Asn | Ile | Lys 120 | Ile | Phe | Glu | Glu | Glu 125 | Glu | Val | Glu |
| 40 | Phe Ile 130 | | Val | Pro | Val | Pro 135 | Glu | Phe | Ala | Asp | Ser 140 | Asp | Pro | Ala | Asn |
| | Ile Val 145 | His | Asp | Phe | Asn 150 | Lys | Lys | Leu | Thr | Ala 155 | Tyr | Leu | Asp | Leu | Asn 160 |
| 45 | Leu Asr | Lys | Cys | Туг 165 | Val | Ile | Pro | Leu | Asn 170 | Thr | Ser | Ile | Val | Met 175 | Pro |
| 50 | Pro Arg | g Asn | Leu 180 | Leu | Glu | Leu | Leu | Ile 185 | Asn | Ile | Lys | Ala | Gly 190 | Thr | Tyr |
| | Leu Pro | 0 Gln 195 | Ser | Tyr | Leu | Ile | His 200 | Glu | His | Met | Val | Ile 205 | Thr | Asp | Arg |
| 55 | Ile Glu 210 | | Ile | Asp | His | Leu 215 | Gly | Phe | Phe | Ile | Tyr 220 | Arg | Leu | Cys | His |
| | Asp Lys 225 | s Glu | Thr | Tyr | Lys 230 | Leu | Gln | Arg | Arg | Glu 235 | Thr | Ile | Lys | Gly | Ile 240 |
| 60 | Gln Ly | s Arg | Glu | Ala | Ser | Asn | Cys | Phe | Ala | Ile | Arg | His | Phe | Glu | Asn |

| | | | | | 245 | | | | | 250 | | | | | 255 | |
|----|------------|------------|---------------------|------------------|-----------------------|------------------------|----------------------|---------------------|--------------------|--------------|------------|------------|------------|------------|------------|------------|
| 5 | Lys | Phe | Ala | Val 260 | Glu | Thr | Leu | Ile | Cys 265 | Ser | Xaa | | | | | |
| 10 | (2) | INFO | CAMAC | | | | | | | : | | | | | | |
| 10 | | | | ~ (. (: (: | A) L: B) T D) T | ENGTI YPE: OPOLA | H: 3 ami: OGY: | 15 a no a lin | mino cid ear | acio | | | | | | |
| 15 | Met | | | | | | | | | EQ II Leu | | | | Thr | Ala | Phe |
| | 1 | T ON | Cor | Lvc | 5 Pro | Thr | Glu | Lve | Luc | 10 Asp | Ara | Va l | Hic | ніс | 15 Glu | Pro |
| 20 | | | | 20 | | | | _ | 25 | | | | | 30 | | |
| | Gln | Leu | Ser 35 | Asp | Lys | Val | His | Asn 40 | Asp | Ala | Gln | Ser | Phe 45 | Asp | Tyr | Asp |
| 25 | His | Asp 50 | Ala | Phe | Leu | Gly | Ala 55 | Glu | Glu | Ala | Lys | Thr 60 | Phe | Asp | Gln | Leu |
| 30 | Thr 65 | Pro | Glu | Glu | Ser | L ys 70 | Glu | Arg | Leu | Gly | Lys 75 | Ile | Val | Ser | Lys | Ile 80 |
| | Asp | Gly | Asp | Lys | Asp 85 | Gly | Phe | Val | Thr | Val 90 | Asp | Glu | Leu | Lys | Asp 95 | Trp |
| 35 | Ile | Lys | Phe | Ala 100 | Gln | Lys | Arg | Trp | Ile 105 | Tyr | Glu | Asp | Val | Glu 110 | Arg | Gln |
| | Trp | Lys | Gly 1 1 5 | His | Asp | Leu | Asn | Glu 120 | Asp | Gly | Leu | Val | Ser 125 | Trp | Glu | Glu |
| 40 | Tyr | Lys 130 | Asn | Ala | Thr | Tyr | Gly 135 | Tyr | Val | Leu | Asp | Asp 140 | Pro | Asp | Pro | Asp |
| 45 | Asp 145 | Gly | Phe | Asn | Tyr | Lys 150 | Gln | Met | Met | Val | Arg 155 | Asp | Glu | Arg | Arg | Phe 160 |
| | Lys | Met | Ala | Asp | Lys 165 | Asp | Gly | Asp | Leu | Ile 170 | Ala | Thr | Lys | Glu | Glu 175 | Phe |
| 50 | Thr | Ala | Phe | Leu 180 | | Pro | Glu | Glu | Туг 185 | Asp | Tyr | Met | Lys | Asp 190 | Ile | Val |
| | Val | Gln | Glu 195 | Thr | Met | Glu | Asp | Ile 200 | Asp | Lys | Asn | Ala | Asp 205 | Gly | Phe | Ile |
| 55 | Asp | Leu 210 | | Glu | Tyr | Ile | Gly 215 | Asp | Met | Tyr | Ser | His 220 | Asp | Gly | Asn | Thr |
| 60 | Asp 225 | | Pro | Glu | Trp | Val 230 | | Thr | Glu | Arg | Glu 235 | | Phe | Val | Glu | Phe 240 |

| | Arg | Asp | Lys | Asn | Arg 245 | Asp | Gly | Lys | Met | Asp 250 | Lys | Glu | Glu | Thr | Lys 255 | Asp |
|----|------------|------------|------------|---------------------|------------------------------|----------------------|-----------------------------|---------------------|---------------------|------------|------------|------------|------------|------------|------------|--------------|
| 5 | Trp | Ile | Leu | Pro 260 | Ser | Asp | Tyr | Asp | His 265 | Ala | Glu | Ala | Glu | Ala 270 | Arg | His |
| | Leu | Val | Tyr 275 | Glu | Ser | Asp | Gln | Asn 280 | Lys | Asp | Gly | Lys | Leu 285 | Thr | Lys | Glu |
| 10 | Glu | Ile 290 | Val | Asp | Lys | Tyr | Asp 295 | Leu | Phe | Val | Gly | Ser 300 | Gln | Ala | Thr | Asp |
| 15 | Phe 305 | Gly | Glu | Ala | Leu | Val 310 | Arg | His | Asp | Glu | Phe 315 | | | | | |
| 20 | (2) | INF | (i) | SEQU () (| ENCE A) L B) T D) T | CHAI ENGT YPE: | RACT H: 2 ami OGY: | 07 a no a lin | TICS mino cid | aci | | . 20 | 5. | | | |
| 25 | Met 1 | Phe | (xi) | | | | | | Leu | | | | | Lys | Asp 15 | Lys |
| 30 | Leu | Val | Asp | Pro 20 | | Leu | Arg | Arg | His 25 | Gly | Leu | Leu | Pro | Ser 30 | Ser | Leu |
| | Lys | Arg | Ile 35 | | Val | Gly | Met | Phe 40 | Phe | Val | Met | Cys | Ser 45 | Ala | Phe | Ala |
| 35 | Ala | Gly 50 | | Leu | Glu | Ser | Lys 55 | | Leu | Asn | Leu | Val 60 | | Glu | Lys | Thr |
| 40 | Ile 65 | | Gln | Thr | Ile | Gly 70 | Asn | Val | Val | Tyr | His 75 | | Ala | Asp | Leu | Ser 80 |
| | | | | | 85 | | | | Leu | 90 | | | | | 95 | |
| 45 | | | | 100 |) | | | | 105 | | | | | 110 | | Lys |
| | | | 115 | 5 | | | | 120 | • | | | | 125 | | | Val |
| 50 | | 130 |) | | | | 135 | 5 | | | | 140 |) | | | : Ala |
| 55 | 145 | 5 | | | | 150 |) | | | | 155 | 5 | | | | 7 Cys 160 |
| | | | | | 165 | 5 | | | | 170 |) | | | | 175 | |
| 60 | Lev | ı Lei | u Le | ı Phe 180 | | ı Ile | e Ile | e Sei | val 185 | | з Туз | Asp | His | His 190 | | J Asp |

| | His | Gln | Arg 195 | Ser | Arg | Ala | Asn | Gly 200 | Val | Pro | Thr | Ser | Arg 205 | Arg | Ala | |
|----|------------|------------|------------|------------|----------------------|------------------------|----------------------|---------------------|---------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | | | | | | | | | | | | | | | | |
| | (2) | INFO | RMAT | NOI | FOR | SEQ | ID 1 | JO: 2 | 206: | | | | | | | |
| 10 | | | | ~ (. (: | A) L B) T D) T | ENGT: YPE : OPOL | H: 1 ami: OGY: | 96 a no a lin | | aci | | : 20 | 5 : | | | |
| 15 | Met 1 | Arg | Ser | Arg | Ile 5 | Arg | Glu | Phe | Asp | Ser 10 | Ser | Thr | Leu | Asn | Glu 15 | Ser |
| 20 | Val | Arg | Asn | Thr 20 | Ile | Met | Arg | Asp | Leu 25 | Lys | Ala | Val | Gly | Lys 30 | Lys | Phe |
| 20 | Met | His | Val 35 | Leu | Tyr | Pro | Arg | Lys 40 | Ser | Asn | Thr | Leu | Leu 45 | Arg | Asp | Trp |
| 25 | Asp | Leu 50 | Trp | Gly | Pro | Leu | Ile 55 | Leu | Cys | Val | Thr | Leu 60 | Ala | Leu | Met | Leu |
| | Gln 65 | Arg | Asp | Ser | Ala | Asp 70 | Ser | Glu | Lys | Asp | Gly 75 | Gly | Pro | Gln | Phe | Ala 80 |
| 30 | Glu | Val | Phe | Val | Ile 85 | Val | Trp | Phe | Gly | Ala 90 | Val | Thr | Ile | Thr | Leu 95 | Asn |
| 35 | Ser | Lys | Leu | Leu 100 | Gly | Gly | Asn | Ile | Ser 105 | Phe | Phe | Gln | Ser | Leu 110 | Cys | Val |
| | Leu | Gly | Туr 115 | Cys | Ile | Leu | Pro | Leu 120 | Thr | Val | Ala | Met | Leu 125 | Ile | Cys | Arg |
| 40 | Leu | Val 130 | | Leu | Ala | Asp | Pro 135 | Gly | Pro | Val | Asn | Phe 140 | Met | Val | Arg | Leu |
| | Phe 145 | Val | Val | Ile | Val | Met 150 | Phe | Ala | Trp | Ser | Ile 155 | Val | Ala | Ser | Thr | Ala 160 |
| 45 | Phe | Leu | Ala | Asp | Ser 165 | Gln | Pro | Pro | Asn | Arg 170 | Arg | Ala | Leu | Ala | Val 175 | Tyr |
| 50 | Pro | Val | Phe | Leu 180 | | Tyr | Phe | Val | Ile 185 | | Trp | Met | Ile | Leu 190 | Thr | Phe |
| 50 | Thr | Pro | Gln 195 | Xaa | | | | | | | | | | | | |
| 55 | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 207: | | | | | | | |
| | | | (i) | | | | | | TICS amino | | ids | | | | | |
| 60 | | | | | (B) 7 | TYPE | : am: | ino a | acid | | | | | | | |

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:

| 5 | Met 1 | Ala | Lys | Asp | Gln 5 | Ala | Val | Glu | Asn | Ile 10 | Leu | Val | Ser | Pro | Val 15 | Val |
|----|--------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|--------------------|------------|------------|------------|------------|------------|
| | Val | Ala | Ser | Ser 20 | Leu | Gly | Leu | Val | Ser 25 | Leu | Gly | Gly | Lys | Ala 30 | Thr | Thr |
| 10 | Ala | Ser | Gln 35 | Ala | Lys | Ala | Val | Leu 40 | Ser | Ala | Glu | Gln | Leú 45 | Arg | Asp | Glu |
| 15 | Glu | Val 50 | His | Ala | Gly | Leu | Gly 55 | Glu | Leu | Leu | Arg | Ser 60 | Leu | Ser | Asn | Ser |
| 13 | Thr 65 | Ala | Arg | Asn | Va1 | Thr 70 | Trp | Lys | Leu | Gly | Ser 75 | Arg | Leu | Tyr | Gly | Pro 80 |
| 20 | Ser | Ser | Val | Ser | Phe 85 | Ala | Asp | Asp | Phe | Val 90 | Arg | Ser | Ser | Lys | Gln 95 | His |
| | Tyr | Asn | Cys | Glu 100 | His | Ser | Lys | Ile | Asn 105 | Phe | Arg | Asp | Lys | Arg 110 | Ser | Ala |
| 25 | Leu | Gln | Ser 115 | Ile | Asn | Glu | Trp | Ala 120 | Ala | Gln | Thr | Thr | Asp 125 | Gly | Lys | Leu |
| 30 | Pro | Glu 130 | Val | Thr | Lys | Asp | Val 135 | Glu | Arg | Thr | Asp | Gly 140 | Ala | Leu | Leu | Val |
| | As n 145 | Ala | Met | Phe | Phe | Lys 150 | Pro | His | Trp | Asp | Glu 1 55 | Lys | Phe | His | His | Lys 160 |
| 35 | Met | Val | Asp | Asn | Arg 165 | Gly | Phe | Met | Val | Thr 170 | Arg | Ser | Tyr | Thr | Val 175 | Gly |
| | Val | Met | Met | Met 180 | His | Arg | Thr | Gly | Leu 185 | Tyr | Asn | Tyr | Tyr | Asp 190 | Asp | Glu |
| 40 | Lys | Glu | Lys 195 | Leu | Gln | Ile | Val | Glu 200 | Met | Pro | Leu | Ala | His 205 | Lys | Leu | Ser |
| 45 | Ser | Leu 210 | Ile | Ile | Leu | Met | Pro 215 | His | His | Val | Glu | Pro 220 | Leu | Glu | Arg | Leu |
| | Glu 225 | Lys | Leu | Leu | Thr | Lys 230 | Glu | Gln | Leu | Lys | 11e 235 | Trp | Met | Gly | Lys | Met 240 |
| 50 | Gln | Lys | Lys | Ala | Val 245 | Ala | Ile | Ser | Leu | Pro 250 | Lys | Gly | Val | Val | Glu 255 | Va] |
| | Thr | His | Asp | Leu 260 | | Lys | His | Leu | Ala 265 | | Leu | Gly | Leu | Thr 270 | Glu | Ala |
| 55 | Ile | Asp | Lys 275 | | Lys | Ala | Asp | Leu 280 | | Arg | Met | Ser | Gly 285 | Lys | Lys | Asp |
| 60 | Leu | Туг 290 | | Ala | Ser | Val | Phe 295 | | Ala | Thr | Ala | Phe 300 | | Leu | Asp | Thu |

| | Asp (| Gly | Asn | Pro | Leu | Thr 310 | Arg | Ile | Thr | Gly | Gly 315 | Gly | Val | Arg | Thr | Gln 320 |
|----|-----------|-----------|-----------|-------------|-----------------------|------------------------|-------------------------------------|-----------------------|--------------------|------------|------------|-----------|-----------|------------|-----------|------------|
| 5. | Val : | Phe | Tyr | Ala | Asp 325 | His | Pro | Phe | Ile | Ser 330 | Xaa | | | | | |
| 10 | (2) | | | SEQUE () | ENCE A) Li B) T | CHAI ENGT: YPE : | ID N RACTE H: 58 amin | ERIST 8 am no a | TICS: ino a | | s | | | | | |
| 15 | | | (xi) | | | | OGY: SCRII | | | EQ II | ON C | : 208 | 3: | | | |
| | Met 1 | Cys | Met | Gln | Leu 5 | Phe | Gly | Phe | Leu | Ala 10 | Phe | Met | Ile | Phe | Met 15 | Cys |
| 20 | Trp | Val | Gly | Asp 20 | Val | Tyr | Pro | Val | Туr 25 | Gln | Pro | Val | Gly | Pro 30 | Lys | Gln |
| 25 | Tyr | Pro | Туr 35 | Asn | Asn | Leu | Tyr | Leu 40 | Glu | Arg | Gly | Gly | Asp 45 | Pro | Ser | Lys |
| | Glu | Pro 50 | Glu | Arg | Val | Val | His 55 | Tyr | Glu | Ile | | | | | | |
| 30 | (2) | INFO | ORMA' | rion | FOR | SEQ | ID 1 | NO: 1 | 209: | | | | | | | |
| 35 | | | | ((| A) L B) T D) T | ENGT YPE : OPOL | RACT H: 3 ami OGY: SCRI | 92 a no a lin | mino cid ear | aci | | : 20 | 9: | | | |
| 40 | Met 1 | Asp | Ala | Leu | Val 5 | Glu | Asp | Asp | Ile | Cys 10 | Ile | Leu | Asn | His | Glu 15 | Lys |
| | Ala | His | Lys | Arg 20 | Asp | Thr | Val | Thr | Pro 25 | Val | Ser | Ile | Tyr | Ser 30 | Gly | Asp |
| 45 | Glu | Ser | Val 35 | | Ser | His | Phe | Ala 40 | | Val | Thr | Ala | Tyr 45 | Glu | Asp | Ile |
| 50 | Lys | Lys 50 | | Leu | Lys | Asp | Ser 55 | | Lys | Glu | Asn | Ser 60 | Leu | Leu | Lys | Lys |
| 50 | Arg 65 | Ile | Arg | Phe | Leu | Glu 70 | | Lys | Leu | Ile | Ala 75 | | Phe | Glu | Glu | 61u 80 |
| 55 | Thr | Ser | Ser | Val | Gly 85 | | Glu | Gln | Val | Asn 90 | | Ala | Tyr | His | Ala 95 | |
| | Arg | Glu | Val | . Cys | | e Asp | Arg | , Asp | Asr 105 | | ı Lys | Ser | Lys | Leu 110 | | Lys |
| 60 | Met | Asn | Lys | . Asp |) Asr | Ser | Glu | ser | Leu | Lys | val | . Leu | Asn | Glu | Glr | ı Leu |

| | | | 115 | | | | | 120 | | | | | 125 | | | |
|----|------------|------------|------------|------------|--------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Gln | Ser 130 | Lys | Glu | Val | Glu | Leu 135 | Leu | Gln | Leu | Arg | Thr 140 | Glu | Val | Glu | Thr |
| 3 | Gln 145 | Gln | Val | Met | Arg | Asn 150 | Leu | Asn | Pro | Pro | Ser 155 | Ser | Asn | Trp | Glu | Val 160 |
| 10 | Glu | Lys | Leu | Ser | Cys 16 5 | Asp | Leu | Lys | Ile | His 170 | Gly | Leu | Glu | Gln | Glu 175 | Leu |
| | Glu | Leu | Met | Arg 180 | Lys | Glu | Cys | Ser | Asp 185 | Leu | Lys | Ile | Glu | Leu 190 | Gln | Lys |
| 15 | Ala | Lys | Gln 195 | Thr | Asp | Pro | Tyr | Gln 200 | Glu | Asp | Asn | Leu | Lys 205 | Ser | Arg | Asp |
| 20 | Leu | Gln 210 | Lys | Leu | Ser | Ile | Ser 215 | Ser | Asp | Asn | Met | Gln 220 | His | Ala | Tyr | Trp |
| | Glu 225 | Leu | Lys | Arg | Glu | Met 230 | Ser | Asn | Leu | His | Leu 235 | Val | Thr | Gln | Val | Gln 240 |
| 25 | Ala | Glu | Leu | Leu | Arg 245 | Lys | Leu | Lys | Thr | Ser 250 | Thr | Ala | Ile | Lys | Lys 255 | Ala |
| | Cys | Ala | Pro | Val 260 | Gly | Cys | Ser | Glu | Asp 265 | Leu | Gly | Arg | Asp | Ser 270 | Thr | Lys |
| 30 | Leu | His | Leu 275 | Met | Asn | Phe | Thr | Ala 280 | Thr | Tyr | Thr | Arg | His 285 | Pro | Pro | Leu |
| 35 | Leu | Pro 290 | Asn | Gly | Lys | Ala | Leu 295 | Cys | His | Thr | Thr | Ser 300 | Ser | Pro | Leu | Pro |
| | Gly 305 | | Val | Lys | Val | Leu 310 | Ser | Glu | Lys | Ala | Ile 315 | Leu | Gln | Ser | Trp | Thr 320 |
| 40 | Asp | Asn | Glu | Arg | Ser 325 | Ile | Pro | Asn | Asp | Gly 330 | Thr | Cys | Phe | Gln | Glu 335 | His |
| | Ser | Ser | Tyr | | Arg | | | Leu | | | | | Trp | Val 350 | | Pro |
| 45 | Ser | Pro | Pro 355 | - | Ser | Ser | Glu | Thr 360 | Ala | Phe | Gly | Glu | Thr 365 | Lys | Thr | Lys |
| 50 | Thr | Leu 370 | | Leu | Pro | Asn | Leu 375 | | Pro | Leu | His | Туr 380 | Leu | Asp | Gln | His |
| | Asn 385 | | Asn | Cys | Leu | Tyr 390 | Lys | Asn | | | | | | | | |
| 55 | (2) | INF | 'ORMA | TION | FOR | SEQ | ID | NO: | 210: | | | | | | | |
| | | | (i) | | | | | ERIS | | | is | | | | | |
| 60 | | | | | (B) T | TYPE: | ami | ino a | cid | | | | | | | |

| | (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 210: | |
|----|---|-----|
| 5 | Met His His His Thr Gln Leu Met Phe Ile Tyr Leu Phe Ile Tyr L 1 5 10 15 | eu |
| | the Ile Leu Gly Val Phe Phe Phe Phe Phe Xaa 20 25 | |
| 10 | | |
| | 2) INFORMATION FOR SEQ ID NO: 211: | |
| 15 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 39 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (Xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211: | |
| 20 | Met Asn Cys Ile Leu Leu Leu Tyr Leu Leu Ile Pro Thr Ile Ser I 1 5 15 | le |
| 25 | Ser Val Val Pro Tyr Val Ala Leu Asn Ile Lys Tyr Ile Lys Glu C 20 25 30 | ys |
| 25 | Thr Glu Asn Ser Phe Tyr Xaa 35 | |
| 30 | (2) INFORMATION FOR SEQ ID NO: 212: | |
| 35 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 71 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212: | |
| 40 | Met Leu Leu His Leu Thr Ala Ala Phe Leu Gln Arg Ala Gln Phe S 1 10 15 | er |
| | Thr Tyr Phe Pro Gly Tyr Phe Asp Gly Gln Tyr Trp Leu Trp Trp V 20 25 30 | /a] |
| 45 | Phe Leu Val Leu Gly Phe Leu Leu Phe Leu Arg Gly Phe Ile Asn 1 35 40 45 | ſŢ |
| 50 | Ala Lys Val Arg Lys Met Pro Glu Thr Phe Ser Asn Leu Pro Arg 50 55 60 | ľhi |
| 30 | Arg Val Leu Phe Ile Tyr Xaa 65 70 | |
| 55 | (2) INFORMATION FOR SEQ ID NO: 213: | |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 83 amino acids | |
| 60 | (B) TYPE: amino acid | |

| | | | (xi) | | | OPOL | | | | EQ II | OM C | : 213 | 3: | | | |
|----|-----------|-----------|-----------|-----------|-------------------------|----------------------|------------------------|-------------------------|----------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 5. | Met 1 | Leu | Thr | Phe | Phe 5 | Met | Ala | Phe | Leu | Phe 10 | Asn | Trp | Ile | Gly | Phe 15 | Phe |
| | Leu | Ser | Phe | Cys 20 | Leu | Thr | Thr | Ser | Ala 25 | Ala | Gly | Arg | Tyr | Gly 30 | Ala | Ile |
| 10 | Ser | Gly | Phe 35 | Gly | Leu | Ser | Leu | Ile 40 | Lys | Trp | Ile | Leu | Ile 45 | Val | Arg | Phe |
| 15 | Ser | Thr 50 | Tyr | Phe | Pro | Ala | Phe 55 | Met | Asn | Ser | Leu | Ser 60 | Arg | Ser | Lys | Arg |
| 13 | Thr 65 | Pro | Ala | Gly | Ser | Glu 70 | Ser | Arg | Cys | Arg | Thr 75 | Gln | Arg | Asn | Asn | His 80 |
| 20 | Leu | Leu | Xaa | | | | | | | | | | | | | |
| | (2) | TNE | ORMA' | PT (M | ΕΩΡ | SEO. | TD I | viO+ · | 2111. | | | | | | | |
| 25 | (2) | TIME | | SEQU | ENCE | СНА | RACT | ERIS | TICS | : acid | S | | | | | |
| | | | | (| в) т | YPE: | ami | no a | cid | acia | | | | | | |
| 30 | | | (xi) | SEQ | | | | | | EQ I | D NC | : 21 | 4: | | | |
| | Met 1 | | Lys | Arg | Ser 5 | Ala | Ser | Phe | Ile | Leu 10 | Leu | Pro | Leu | Leu | Phe 15 | Leu |
| 35 | Lys | Gly | Ser | Phe 20 | Ala | Lys | Leu | Asn | Ala 25 | | Ile | Ser | Asp | Cys 30 | Leu | Glu |
| 40 | Glu | Arg | Туr 35 | Cys | His | Asn | Leu | Trp 40 | | Val | Phe | Gln | Gly 45 | Cys | Val | Il∈ |
| 40 | Thr | Glu 50 | Leu | His | Leu | Ser | Arg 55 | | Ser | Lys | Thr | Leu 60 | | Ser | Leu | Cys |
| 45 | Туг 65 | | Phe | Val | Ile | Asn 70 | | Tyr | Ile | Phe | Phe 75 | | Phe | Leu | Asp | 11e |
| | Thr | • | | | | | | | | | | | | | | |
| 50 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA | TION | FOF | SEÇ |] ID | NO: | 215: | | | | | | | |
| 55 | | | (i) | | (A) : (B) ' (D) ' | LENG TYPE TOPO | TH: 4 : am: LOGY | 19 ar ino a : lir | mino acid near | acio | | | | | | |
| | | | (xi) | | | | | | | SEQ : | | | | | | |
| 60 | Met | c Cys | Ser | Leu | ı Ph∈ | e Glu | ı Ser | Arg | j Phe | e Phe | e Cys | s Phe | e Val | . Let | ı Ph∈ | e Se |

| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
|----|------------|------------|------------|------------|------------|--------------|--------------|-----------------------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | Glu | Lys | Ile | Ile 20 | Gln | Leu | Cys | Ala | Ser 25 | Ile | Ala | Phe | Leu | Cys 30 | Phe | Val |
| 5 | Lys | His | Val 35 | Pro | Trp | Pro | Lys | Trp 40 | Lys | Arg | Lys | Cys | Leu 45 | Ile | Asn | Ala |
| 10 | Phe | | | | | | | | | | | | | | | |
| 15 | (2) | | ORMAT | | | | | NO: 2 | | : | | | | | | |
| 20 | | | (xi) | (1 | B) T | YPE: OPOL | ami: OGY: | 03 a no a lin PTIO | cid ear | | | : 210 | 5 : | | | |
| | Met 1 | Thr | Leu | Arg | Pro 5 | Ser | Leu | Leu | Pro | Leu 10 | His | Leu | Leu | Leu | Leu 15 | Leu |
| 25 | Leu | Leu | Ser | Ala 20 | Ala | Val | Cys | Arg | Ala 25 | Glu | Ala | Gly | Leu | Glu 30 | Thr | Glu |
| 30 | Ser | Pro | Val 35 | Arg | Thr | Leu | Gln | Val 40 | Glu | Thr | Leu | Val | Glu 45 | Pro | Pro | Glu |
| 30 | Pro | Cys 50 | Ala | Glu | Pro | Ala | Ala 55 | Phe | Gly | Asp | Thr | Leu 60 | His | Ile | His | Tyr |
| 35 | Thr 65 | Gly | Ser | Leu | Val | Asp 70 | Gly | Arg | Ile | Ile | Asp 75 | Thr | Ser | Leu | Thr | Arg 80 |
| | Asp | Pro | Leu | Val | Ile 85 | Glu | Leu | Gly | Gln | Lys 90 | Gln | Val | Ile | Pro | Gly 95 | Leu |
| 40 | Glu | Gln | Ser | Leu 100 | Leu | Asp | Met | Cys | Val 105 | Gly | Glu | Lys | Arg | Arg 110 | Ala | Ile |
| 45 | Ile | Pro | Ser 115 | His | Leu | Ala | Tyr | Gly 120 | Lys | Arg | Gly | Phe | Pro 125 | Pro | Ser | Val |
| | Pro | Ala 130 | Asp | Ala | Val | Val | Gln 135 | Туr | Asp | Val | Glu | Leu 140 | Ile | Ala | Leu | Ile |
| 50 | Arg 145 | | Asn | Tyr | Trp | Leu 150 | Lys | Leu | Val | Lys | Gly 155 | Ile | Leu | Pro | Leu | Val 160 |
| | Gly | Met | Ala | Met | Val 165 | | Pro | Ser | Trp | Ala 170 | | Leu | Gly | Ile | Thr 175 | |
| 55 | Thr | Glu | Arg | Pro 180 | | Asp | Pro | Lys | Ser 185 | | Lys | Arg | Ser | Ser 190 | | Lys |
| 60 | Arg | Asn | Glu 195 | | Arg | Ala | Lys | Arg 200 | | Asn | Lys | | | | | |

| | (2) | INFO | PAMA | NOI | FOR | SEQ | ID N | 10: 2 | 217: | | | | | | | |
|------------|------------|------------|------------|------------|----------------------|----------------------|---------------------|-------------------------|--------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | | | | (1 (1 | A) L B) T D) T | ENGT YPE: OPOL | H: 1 ami OGY: | 86 ai no a line | ear | acio | | . 211 | 7. | | | |
| 10 | Met 1 | | | | | | | | N: SI Pro | | | | | Leu | Val 15 | Phe |
| 15 | Ser | Ile | Ser | Leu 20 | Trp | Ile | Ile | Ala | A1a 25 | Trp | Thr | Val | Arg | Val 30 | Cys | Glu |
| | Ser | Pro | Glu 35 | Ser | Pro | Ala | Gln | Pro 40 | Ser | Gly | Ser | Ser | Leu 45 | Pro | Ala | Trp |
| 20 | Tyr | His 50 | Asp | Gln | Gln | Asp | Val 55 | Thr | Ser | Asn | Phe | Leu 60 | Gly | Ala | Met | Trp |
| 25 | Leu 65 | Ile | Ser | Ile | Thr | Phe 70 | Leu | Ser | Ile | Gly | Туг 75 | Gly | Asp | Met | Val | Pro 80 |
| - 5 | His | Thr | Tyr | Cys | Gly 85 | Lys | Gly | Val | Cys | Leu 90 | Leu | Thr | Gly | Ile | Met 95 | Gly |
| 30 | Ala | Gly | Cys | Thr 100 | Ala | Leu | Val | Val | Ala 105 | Val | Val | Ala | Arg | Lys 110 | Leu | Glu |
| | Leu | Thr | Lys 115 | Ala | Glu | Lys | His | Val 120 | His | Xaa | Phe | Met | Met 125 | Asp | Thr | Gln |
| 35 | Leu | Thr 130 | | Arg | Ile | Lys | Asn 135 | Xaa | Ala | Ala | Asn | Val 140 | Leu | Xaa | Glu | Thr |
| 40 | Trp 145 | Leu | Ile | Tyr | Lys | His 1 50 | Thr | Lys | Leu | Leu | Lys 155 | Lys | Ile | Asp | His | Ala 160 |
| 10 | Lys | Val | Arg | Asn | Thr 165 | Arg | Gly | Ser | Ser | Ser 170 | Lys | Tyr | Pro | Pro | Val 175 | Glu |
| 45 | Glu | Arg | Gln | Asp 180 | Gly | Thr | Glu | Glu | Ala 185 | Glu | | | | | | |
| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 218: | | | | | | | |
| 50 | | | (i) | | | | | | TICS nino | | ls | | | | | |
| 55 | | | (xi) | (| (D) 1 | OPOI | OGY: | ino a : lir :PTIC | | SEQ I | D NO |): 21 | .8: | | | |
| | Met 1 | | : Phe | : Leu | Ala 5 | | Leu | Val | Leu | Leu 10 | | Val | Ser | Ile | Phe | Let |
| 60 | Va1 | Ser | · Ala | Gln | Asn | Pro | Thr | Thr | · Ala | Ala | Pro | Ala | Asp | Thr | Tvr | Pro |

| | | | | 20 | | | | | 25 | | | | | 30 | | |
|----|-----------|-----------|------------|------------|----------------|-----------|-------------|--------------------------------|------------|-----------|-----------|-----------|------------|------------|-----------|-----------|
| _ | Ala | Thr | Gly 35 | Pro | Ala | Asp | Asp | Glu 40 | Ala | Pro | Asp | Ala | Glu 45 | Thr | Thr | Ala |
| 5 | Ala | Ala 50 | Thr | Thr | Ala | Thr | Thr 55 | Ala | Ala | Pro | Thr | Thr 60 | Ala | Thr | Thr | Ala |
| 10 | Ala 65 | Ser | Thr | Thr | Ala | Arg 70 | Lys | Asp | Ile | Pro | Val 75 | Leu | Pro | Lys | Trp | Val 80 |
| | Gly | Asp | Leu | Pro | Asn 85 | Gly | Arg | Val | Cys | Pro 90 | | | | | | |
| 15 | | | | | | | | | 210 | | | | | | | |
| | (2) | | | | | | | NO: 2 ERIS | | : | | | | | | |
| 20 | | | (xi) | (| B) T D) T | YPE: | ami OGY: | 39 a no a lin PTIO | cid ear | | | : 21 | 9 : | | | |
| 25 | Met 1 | Ser | Ser | Ala | Ala 5 | Ala | Asp | His | Trp | Ala 10 | Trp | Leu | Leu | Val | Leu 15 | Ser |
| 30 | Phe | Val | Phe | Gly 20 | Cys | Asn | Val | Leu | Arg 25 | Ile | Leu | Leu | Pro | Ser 30 | Phe | Ser |
| 50 | Ser | Phe | Met 35 | Ser | Arg | Val | Leu | Gln 40 | Lys | Asp | Ala | Glu | Gln 45 | Glu | Ser | Glr |
| 35 | Met | Arg 50 | | Glu | Ile | Gln | Asp 55 | Met | Lys | Gln | Glu | Leu 60 | Ser | Thr | Val | Asr |
| | Met 65 | | Asp | Glu | Phe | Ala 70 | | Tyr | Ala | Arg | Leu 75 | Glu | Arg | Lys | Ile | Asr 80 |
| 40 | Lys | Met | Thr | Asp | Lys 85 | Leu | Lys | Thr | His | Val 90 | Lys | Ala | Arg | Thr | Ala 95 | Glr |
| 45 | Leu | Ala | Lys | Ile 100 | | Trp | Val | Ile | Ser 105 | | Ala | Phe | Tyr | Val 110 | Leu | Glr |
| | Ala | Ala | Leu 115 | | Ile | Ser | Leu | 11e 120 | | Lys | Tyr | Tyr | Ser 125 | | Pro | Va] |
| 50 | Ala | Val | | Pro | Ser | Lys | Trp 135 | Ile | Thr | Leu | Xaa | | | | | |
| 55 | (2) | INF | | SEQU | JENCE (A) I | E CHA | ARACI | NO: TERIS 48 ar ino a | TICS | | ds | | | | | |
| 60 | | | (xi) | | (D) | ropo: | LOGY | : lin | near | SEQ I | D NO | o: 22 | 20: | | | |

PCT/US98/05311

| | Met 1 | Ser | Ser | Ala | Ala 5 | Ala | Asp | His | Trp | Ala 10 | Trp | Leu | Leu | Val | Leu 15 | Ser |
|----|-----------|-------------|-------------|-----------|-------------------------|--------------------------|------------------------|-------------------------|----------------------|-----------|-------|-----------|-----------|-----------|-----------|-------|
| 5 | Phe | Val | Phe | Gly 20 | Cys | Asn | Val | Leu | Arg 25 | Ile | Leu | Leu | Pro | Ser 30 | Phe | Ser |
| 10 | Ser | Phe | Met 35 | Ser | Arg | Val | Leu | Gln 40 | Lys | Asp | Ala | Asp | Arg 45 | Ser | His | Arg |
| 15 | (2) | INF | ORMA' | rion | FOR | SEQ | ID I | NO: 2 | 221: | | | | | | | |
| 20 | | | | (| A) L B) T D) T | ENGT YPE : OPOL | H: 7 ami OGY: | 0 am no a lin | ino cid ear | acid | | : 22 | 1: | | | |
| 25 | Met 1 | Thr | Ala | Pro | Leu 5 | Pro | Pro | Leu | Ser | Gly 10 | Leu | Ala | Leu | Phe | Leu 15 | Ile |
| | Val | Phe | Phe | Ser 20 | Leu | Gly | Val | Phe | Cys 25 | Ile | Cys | His | Ser | His 30 | Trp | Tyr |
| 30 | His | Thr | Leu 35 | Gln | Gln | Met | Ala | Gly 40 | Thr | Glu | Pro | Lys | Ala 45 | Leu | Leu | Leu |
| 35 | Ser | Pro 50 | | Ala | Ala | Thr | Thr 55 | | Val | Thr | Val | Thr 60 | His | Glu | Val | Trp |
| | Lys 65 | | Gln | Ala | Leu | Ala 70 | | | | | | | | | | |
| 40 | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 222: | | | | | | | |
| 45 | | | | | (A) I (B) ! (D) ! | LENGT TYPE : TOPOI | TH: 8 : am: LOGY | 33 ar ino a : lir | mino acid near | ació | | o: 22 | :2: | | | |
| 50 | Met 1 | | Cys | : Ser | Val | | Leu | Leu | . Leu | Ile 10 | | ı Gly | Leu | Arg | Cys 15 | |
| | Gly | v Val | L Arc | Pro 20 | | Leu | ι Va] | . Gly | / Glu 25 | | His | s Asn | Pro | Ser 30 | | Leu |
| 55 | Val | L Cys | s Leu 35 | | Leu | Lys | : Asp | Ser 40 | | Thr | Asr | n Glr | Gly 45 | | Cys | Pro |
| 60 | Gl | / Gly 50 | | Trp | Se1 | Glu | a Arg | | o Ile | e Glu | ı Sei | c Val | | : Ser | Asp |) Asn |

| | Cys (| Glu | Ala' | Thr : | Leu (| Gly ' 70 | ryr . | Arg i | Asn 1 | His S | Ser : 75 | Leu | Pro | Ser | Asn ' | Tyr 80 |
|---------------------------------|-------------------------|--------------------------------|-------------------------|--|--------------------------------|-------------------------|-------------------------|-------------------------|--------------------------------|--------------------------------|-------------------------|-------------------------|--------------------------------|--------------------------------|---------------------------------------|--------------------------------|
| 5 | Tyr A | ∖ sn | Ser | | | | | | | | | | | | | |
| 10 | (2) | | | EQUE (<i>P</i> | NCE | CHAR INGTH PE: | ACTE I: 43 amir | O: 2: RIST ami | ICS: no a | ıcids | : | | | | | |
| 15 | | (| xi) | | | | | line TION | | Q ID | NO: | 223 | : | | | |
| | Met 1 | Ĺeu | Thr | Arg | Ser 5 | Leu | Lys | Thr | Leu | Pro 10 | Ser | Ala | Cys | Thr | Ala 15 | Phe |
| 20 | Leu : | Leu | Leu | Phe 20 | Phe | Leu | Phe | Ser | Ser 25 | Gly | Asp | Pro | Glu | Leu 30 | Ser | Cys |
| 25 | Ser | Суз | Thr 35 | Leu | Arg | Thr | Gln | Ser 40 | Ser | Trp | Ser | | | | | |
| | (2) | INFO | RMAT | OION | FOR | SEQ | ID N | JO: 2 | 24: | | | | | | | |
| 30 | | | (i) S | () () | A) L: 3) T | ENGTI YPE : | H: 1: ami | ERIST 84 ar no ac | mino cid | | ds | | | | | |
| 25 | | | (xi) | | | | | line PTION | | EQ II | ON C | : 224 | 1: | | | |
| 35 | Met 1 | Trp | Arg | Pro | Ser 5 | Val | Leu | Leu | Leu | Leu 10 | Leu | Leu | Leu | Arg | His 15 | Gly |
| 40 | Ala | Gln | Gly | Lys 20 | Pro | Ser | Pro | Asp | Δla | | | | _ | | ~ 7 | |
| | | | | 20 | | | | | 25 | Gly | Pro | His | Gly | 30 | GIA | Arg |
| | Val | His | Gln 35 | | Ala | Pro | Leu | Ser 40 | 25 | | | | | 30 | | |
| 45 | | | 35 | Ala | | | | Ser | 25 Asp | Ala | Pro | His | Asp 45 | 30 Asp | Ala | His |
| | Gly | Asn 50 | 35 Phe | Ala Gln | Tyr | Asp | His 55 | Ser 40 | 25 Asp Ala | Ala Phe | Pro Leu | His Gly 60 | Asp 45 Arg | 30 Asp Glu | Ala Val | His Ala |
| 4550 | Gly Lys 65 | Asn 50 Glu | 35 Phe Phe | Ala Gln Asp | Tyr Gln | Asp Leu 70 | His 55 Thr | Ser 40 Glu | 25 Asp Ala Glu | Ala Phe Glu | Pro Leu Ser 75 | His Gly 60 Gln | Asp 45 Arg Ala | 30 Asp Glu Arg | Ala Val Leu | His Ala Gly 80 |
| | Gly Lys 65 Arg | Asn 50 Glu Ile | 35 Phe Phe Val | Ala Gln Asp | Tyr Gln Arg 85 | Asp Leu 70 Met | His 55 Thr | Ser 40 Glu Pro | 25 Asp Ala Glu Ala | Ala Phe Glu Gly 90 | Pro Leu Ser 75 Asp | His Gly 60 Gln | Asp 45 Arg Ala Asp | 30 Asp Glu Arg | Ala Val Leu Trp 95 Arg | His Ala Gly 80 Val |
| 50 | Gly Lys 65 Arg | Asn 50 Glu Ile Leu | 35 Phe Phe Val | Ala Gln Asp Asp Glu 100 | Tyr Gln Arg 85 Leu | Asp Leu 70 Met | His 55 Thr Asp | Ser 40 Glu Pro | 25 Asp Ala Glu Ala Ile 105 | Ala Phe Glu Gly 90 Ala | Pro Leu Ser 75 Asp | His Gly 60 Gln Gly Thr | Asp 45 Arg Ala Asp | 30 Asp Glu Arg Gly Gln 110 Thr | Ala Val Leu Trp 95 Arg | His Ala Gly 80 Val |

| | | 130 | | | | | 135 | | | | | 140 | | | | |
|----|------------|-----------|-----------|----------------|-------------------------|------------------------|------------------------|----------------------------|-----------------------|------------|------------|-----------|--------------|-----------|------------|------------|
| 5 | Xaa 145 | Xaa | Pro | Xaa | Glu | Glu 150 | Phe | His | Asp | Val | Glu 155 | Asp | Ala | Glu | Thr | Ту1 160 |
| 3 | Lys | Lys | Met | Leu | Xaa 165 | Arg | Asp | Glu | Arg | Arg 170 | Phe | Arg | Val | Ala | Asp 175 | Glr |
| 10 | Asp | Gly | Asp | Ser 180 | Met | Ala | Thr | Arg | | | | | | | | |
| 15 | (2) | INF | ORMA(| SEQU)) | ENCE A) L B) T | CHA ENGT YPE: | RACT H: 7 ami | ERIS 1 am | TICS ino cid | | s | | | | | |
| 20 | | | (xi) | | | | | lin PTIO | | EQ I | D NO | : 22 | 5 : | | | |
| | Met 1 | Trp | Leu | Phe | Ile 5 | Leu | Leu | Ser | Leu | Ala 10 | Leu | Ile | Ser | Asp | Ala 15 | Met |
| 25 | Val | Met | Asp | Glu 20 | Lys | Val | Lys | Arg | Ser 25 | Leu | Cys | Trp | Thr | Arg 30 | Leu | Le |
| 30 | Pro | Ser | Ala 35 | Thr | Thr | Met | Pro | Xaa 40 | Thr | Arg | Ile | Thr | Pro 45 | Asn | Thr | Gly |
| | Ala | Glu 50 | Xaa | Ile | Ser | Val | Xaa 55 | Thr | Ala | Thr | Ser | Ser 60 | Pro | Ser | Pro | Le |
| 35 | Thr 65 | | Pro | Ile | Met | Trp 70 | Pro | | | | | | | | | |
| 40 | (2) | INF | ORMA | SEQU | ENCE | СНА | RACT | NO: ERIS | TICS | | le. | | | | | |
| 45 | | | (xi) | (| (B) 1 | YPE : | ami OGY: | ino a lino a lir | acid near | | | o: 22 | 6: | | | |
| | Met 1 | | Val | Phe | Val | | Glu | Ile | Phe | Leu 10 | | | | | | |
| 50 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 2 27 : | | | | | | | |
| 55 | | | | | (A) I (B) 7 (D) 7 | LENG: FYPE FOPOI | TH: : : am: LOGY | TERIS 138 a ino a : lin | amino acid near | o aci | |): 22 | : 7 : | | | |
| 60 | Met | : Ala | . Val | | | | | | | | | | | Leu | Ala | . Le |

| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
|-----------|-----------|------------|-------------|------------|--|-----------------------|---------------------|-------------------------|---------------------|-----------|-----------|-----------|------------|------------|-----------|-----------|
| 5 | Thr | Phe | Ile | Thr 20 | Asp | Asn | Ser | Leu | Val 25 | Ala | Ala | Gly | His | Asp 30 | Cys | Phe |
| 3 | Pro | Val | Leu 35 | Phe | Thr | Tyr | Asp | Ala 40 | Ala | Ala | Gly | Met | Leu 45 | Ser | Phe | Gly |
| 10 | Gly | Arg 50 | Leu | Asp | Val | Pro | Lys 55 | Gln | Ser | Ser | Gln | Arg 60 | Gly | Leu | Thr | Ala |
| | Arg 65 | Glu | Arg | Phe | Gln | Asn 70 | Leu | Asp | Lys | Lys | Ala 75 | Ser | Ser | Glu | Gly | Gly 80 |
| 15 | Thr | Ala | Ala | Gly | Ala 85 | Gly | Leu | Asp | Ser | Leu 90 | His | Lys | Asn | Ser | Val 95 | Ser |
| 20 | Gln | Ile | Ser | Val 100 | Leu | Ser | Gly | Gly | Lys 105 | Ala | Lys | Cys | Ser | Gln 110 | Phe | Cys |
| 20 | Thr | Thr | Gly 115 | Met | Asp | Gly | Gly | Met 120 | Ser | Ile | Trp | Asp | Val 125 | Lys | Ser | Leu |
| 25 | Glu | Ser 130 | Ala | Leu | Lys | Asp | Leu 135 | Lys | Ile | Lys | | | | | | |
| 30 | (2) | INF | ORMA! | | FOR ENCE | | | | | : | | | | | | |
| - | | | | (| A) LB) TD) T | YPE: | ami | no a | cid | acid | ls | | | | | |
| 35 | | | (xi) | SEQ | UENC | E DE | SCRI | PTIO | N: S | EQ I | D NO | : 22 | 8: | | | |
| | Leu 1 | Gly | Ser | Leu | Ser 5 | Thr | Ala | Pro | Ser | Ser 10 | Ala | Leu | Pro | Thr | Leu 15 | Gly |
| 40 | Ala | Arg | Arg | Thr 20 | Arg | Ser | Lys | | | | | | | | | |
| 45 | (2) | INF | ORMA | TION | FOR | SEQ | ID: | NO: | 229: | | | | | | | |
| 50 | | | (i) (xi) | (| ENCE (A) I (B) I (D) I | ENGT YPE : YPOI | H: 1 ami OGY: | l33 a ino a : lir | mind cid near | aci | |): 22 | .9 : | | | |
| 55 | Met 1 | | Tyr | Phe | Ser 5 | | Leu | Leu | Val | Ile 10 | | Ala | Phe | Ala | Ala 15 | Trp |
| <i>33</i> | Val | Ala | Leu | Ala 20 | | Gly | Leu | Gly | Val 25 | | . Val | Туг | Ala | Ala 30 | Ala | Val |
| 60 | Leu | Leu | Gly 35 | | Gly | Cys | Ala | Thr | | . Leu | Val | Thr | Ser 45 | | Ala | Met |

| | Thr | Ala 50 | Asp | Leu | Ile | Gly | Pro 55 | His | Thr | Asn | Ser | Gly 60 | Ala | Phe | Val | Tyr |
|----|-----------|------------|------------|------------|----------------------|------------------------|---------------------|---------------------|------------|-----------|-----------|-----------|------------|------------|-----------|-----------|
| 5 | Gly 65 | Ser | Met | Ser | Phe | Leu 70 | Asp | Lys | Val | Ala | Asn 75 | Gly | Leu | Ala | Val | Met 80 |
| 10 | Ala | Ile | Gln | Ser | Leu 85 | His | Pro | Cys | Pro | Ser 90 | Glu | Leu | Cys | Cys | Arg 95 | Ala |
| 10 | Cys | Val | Ser | Phe 100 | Tyr | His | Trp | Ala | Met 105 | Val | Ala | Val | Thr | Gly 110 | Gly | Val |
| 15 | Gly | Val | Ala 115 | Ala | Ala | .Leu | Cys | Leu 120 | Cys | Ser | Leu | Leu | Leu 125 | Trp | Pro | Thr |
| | Arg | Leu 130 | Arg | Arg | Xaa | | | | | | | | | | | |
| 20 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA | rion | FOR | SEQ | ID I | NO: 2 | 230: | | | | | | | |
| 25 | | | | - (| A) L B) T D) T | ENGT YPE : 'OPOL | H: 2 ami OGY: | 8 am no a lin | | acid | | : 23 | 0: | | | |
| 30 | Gly 1 | Lys | Pro | Thr | Gly 5 | Lys | Ser | Leu | Pro | Leu 10 | Met | Trp | Met | Ile | Leu 15 | Met |
| 35 | Gln | Pro | Ile | Ile 20 | Met | Ile | Ser | Met | Met 25 | Ser | Asn | Gly | | | | |
| | (2) | INF | ORMA' | TION | FOR | SEQ | ID : | NO: | 231: | | | | | | | |
| 40 | | | (i) | (| A) I B) I | ENGT YPE: | H: 6 | | | | ls | | | | | |
| 45 | | | (xi) | | | | | | N: S | EQ I | D NO | : 23 | 1: | | | |
| 45 | Met 1 | | Gly | Lys | Phe 5 | Met | Lys | Val | Gln | Val 10 | Tyr | Arg | Phe | Leu | Lys 15 | Tyr |
| 50 | Leu | Leu | Met | Leu 20 | Leu | Cys | Met | Phe | Val 25 | Asn | Arg | Gly | Met | Ser 30 | Lys | Asp |
| | Ser | Thr | Lys 35 | _ | Pro | Gly | Gln | Glu 40 | Lys | Leu | Lys | Val | Ser 45 | Leu | Gly | Ser |
| 55 | Ile | Leu 50 | Asn | Met | Lys | Ser | Gln 55 | _ | Pro | Leu | Ser | Trp 60 | _ | | | |
| 60 | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 232: | | | | | | | |

```
(i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 29 amino acids
                    (B) TYPE: amino acid
 5
                    (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 232:
     Met Met Glu Arg Ser Met Met Ile Leu Leu Met Ala Ala Ser Met Thr
10
     Met Thr Ser Thr Gln Leu Trp Ser Phe Cys Cys Val His
15
      (2) INFORMATION FOR SEQ ID NO: 233:
             (i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 18 amino acids
20
                     (B) TYPE: amino acid
                    (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 233:
      Met Trp Tyr Gln Leu Ala Lys Glu Glu Pro Gly Val Gly Ala Cys Ala
25
      Leu Asp
30
      (2) INFORMATION FOR SEQ ID NO: 234:
             (i) SEQUENCE CHARACTERISTICS:
35
                     (A) LENGTH: 2 amino acids
                     (B) TYPE: amino acid
                     (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 234:
40
      Leu Xaa
       . 1
45
      (2) INFORMATION FOR SEQ ID NO: 235:
              (i) SEQUENCE CHARACTERISTICS:
                     (A) LENGTH: 72 amino acids
                     (B) TYPE: amino acid
50
                     (D) TOPOLOGY: linear
              (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 235:
      Met Leu Ile Cys Arg Leu Val Leu Leu Ala Asp Pro Gly Pro Val Asn
55
      Phe Met Val Arg Leu Phe Val Val Ile Val Met Phe Ala Trp Ser Ile
                                        25
                   20
      Val Ala Ser Thr Ala Phe Leu Ala Asp Ser Gln Pro Pro Asn Arg Arg
60
                                    40
               35
```

| | Ala | Leu 50 | Ala | Val | Tyr | Pro | Val 55 | Phe | Leu | Phe | Tyr | Phe 60 | Val | Ile | Ser | Trp |
|----|-----------|-----------------|-------------|-----------|-----------------------------|-------------------------|-------------------------|---|----------------------|-----------|-----------|---------------|-----------|-----------|-----------|-----------|
| 5 | Met 65 | Ile | Leu | Thr | Phe | Thr 70 | Pro | Gln | | | | | | | | |
| 10 | (2) | INF | ORMA' | rion | FOR | SEQ | ID 1 | NO: 2 | 236: | | | | | | | |
| 15 | | | | (| A) L B) T D) T | ENGT YPE : OPOL | H: 9 ami OGY: | ERIST 6 am no a lin PTIO | ino a cid ear | acid | | : 23 | 6: | | | |
| 20 | Met 1 | Arg | Ser | Leu | Leu 5 | Leu | Leu | Ser | Ala | Phe 10 | Cys | Leu | Leu | Glu | Ala 15 | Ala |
| 20 | Leu | Ala | Ala | Glu 20 | Val | Lys | Lys | Pro | Ala 25 | Ala | Ala | Ala | Ala | Pro 30 | Gly | Thr |
| 25 | Ala | Glu | Lys 35 | Leu | Ser | Pro | Lys | Ala 40 | Ala | Thr | Leu | Ala | Glu 45 | Arg | Xaa | Pro |
| | Ala | Trp 50 | Pro | Ser | Ala | Cys | Thr 55 | Arg | Pro | Trp | Pro | Arg 60 | Thr | Arg | Gln | Trp |
| 30 | Arg 65 | Thr | Ser | Trp | Cys | His 70 | Pro | Trp | Trp | Trp | Pro 75 | Arg | Arg | Trp | Gly | Ser 80 |
| 35 | Cys | Arg | Trp | Ala | Ala 85 | Arg | Arg | Pro | Arg | Arg 90 | Arg | Arg | Pro | Arg | Gln 95 | Cys |
| 40 | (2) | INF | | | | | | NO: | | | | | | | | |
| 45 | | | | - 1 | (A) I (B) I (D) I | ENGT TYPE : TOPOI | TH: 1 : ami LOGY: | PERIS 143 a ino a : lir IPTIC | mino acid near | aci | |): 2 3 | .7 : | | | |
| 50 | Met 1 | | , Ser | Leu | Leu 5 | | . Leu | Ser | Ala | Phe 10 | | Leu | Leu | Glu | Ala 15 | |
| | Leu | ı Ala | a Ala | Glu 20 | | Lys | Lys | Pro | Ala 25 | | Ala | Ala | Ala | Pro | | Thr |
| 55 | Ala | Glu | ı Lys 35 | | Ser | Pro | Lys | Ala | | Thr | Leu | Ala | Glu 45 | | Lys | Arg |
| 60 | Pro | Gl ₃ | | ı Glr | Leu | ı Val | Pro 55 | Gly | His | Gly | Gln | Gly 60 | | Gly | Ser | Gly |

| | Glu 65 | His | Pro | Gly | Val | Thr 70 | Arg | Gly | Gly | Gly | Leu 75 | Val | Ala | Gly | Ala | Arg 80 |
|----|-----------|------------|------------|---------------------|------------------------------|---------------------|------------------------------|------------------------------|---------------------|-----------|-----------|------------|------------|------------|-----------|-----------|
| 5 | Val | Ala | Gly | Arg | Gln 85 | Gly | Asp | His | Gly | Val 90 | Ala | Gly | Gln | Gly | Ser 95 | Alā |
| | Glu | Arg | Arg | Ala 100 | Ala | Ala | Arg | Arg | Gly 105 | Gly | Ala | Arg | Arg | Pro 110 | Gly | Arg |
| 10 | Ala | Ala | Ala 115 | Leu | Thr | Gln | Gln | Leu 120 | His | Gly | Ala | Gln | Arg 125 | Asp | Leu | Glu |
| 15 | Ala | Gly 130 | Gln | Pro | Thr | Val | Arg 135 | Thr | Gln | Leu | Ser | Glu 140 | Leu | Arg | Xaa | |
| 20 | (2) | | | SEQU))) | ENCE A) L B) T D) T | CHA ENGT YPE: | RACT: H: 1 ami OGY: | ERIS' 42 a no a lin | FICS mino cid | aci | | : 23 | 8: | | | |
| 25 | Met 1 | Arg | | - | | | | | | | | | | Glu | Ala 15 | Alá |
| 30 | Leu | Ala | Ala | Glu 20 | Va1 | Lys | Lys | Pro | Ala 25 | Ala | Ala | Ala | Ala | Pro 30 | Gly | Thi |
| | Ala | Glu | Lys 35 | Leu | Ser | Pro | Lys | Ala 40 | Ala | Thr | Leu | Ala | Glu 45 | Arg | Xaa | Arg |
| 35 | Pro | Gly 50 | | Gln | Leu | Val | Pro 55 | Gly | His | Gly | Gln | Gly 60 | Pro | Gly | Ser | Gly |
| 40 | Glu 65 | His | Pro | Gly | Val | Thr 70 | Arg | Gly | Gly | Gly | Leu 75 | Val | Ala | Gly | Ala | Arg 80 |
| | Val | Ala | Gly | Arg | Gln 85 | Gly | Asp | His | Gly | Val 90 | Ala | Gly | Gln | Gly | Ser 95 | Ala |
| 45 | Glu | Arg | Arg | Ala 100 | Ala | Ala | Arg | Arg | Gly 105 | Gly | Ala | Arg | Arg | Pro 110 | Gly | Arg |
| | Ala | Ala | Ala 115 | | Thr | Gln | Gln | Leu 120 | | Gly | Ala | Gln | Arg 125 | | Leu | Gl |
| 50 | Ala | Gly 130 | | Pro | Thr | Val | Arg 135 | | Gln | Leu | Ser | Glu 140 | | Arg | | |
| 55 | (2) | INF | | | | | | | 239: TICS | S: | | | | | | |
| 60 | | | - | | (A) I (B) 7 | ENGT | TH: 5 | | nino acid | | is | | | | | |

| | | | (X1) | SEQU | JENCE | DES | CKII | -T-T-OI | 4: SI | ZQ II | טעו כ | . 23: | <i>7</i> : | | | |
|----|----------|-------------|-----------|-----------|-------------------------|------------------------|----------------------|---------------------|-------------------|-----------|-------|-----------|------------|-----------|-----------|-----|
| 5 | Asp 1 | Pro | Glu | Ala | Ala 5 | Asp | Ser | Gly | Glu | Pro 10 | Gln | Asn | Lys | Arg | Thr 15 | Pro |
| J | Asp | Leu | Pro | Glu 20 | Glu | Glu | Tyr | Val | Lys 25 | Glu | Glu | Ile | Gln | Glu 30 | Asn | Glu |
| 10 | Glu | Ala | Val 35 | Lys | Lys | Met | Leu | Val 40 | Glu | Ala | Thr | Arg | Glu 45 | Phe | Glu | Glu |
| | Val | Val 50 | Val | Asp | Glu | Ser | | | | | | | | | | |
| 15 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA! | rion | FOR | SEQ | ID N | NO: 2 | 240: | | | | | | | |
| 20 | | | | (| A) L: B) T' D) T' | ENGT: YPE : OPOL | H: 6 ami: OGY: | 3 am no a lin | ino cid ear | acid | | : 24 | 0: | | | |
| 25 | Cln | Lvc | Len | Lare | Δτα | Lve | Δla | Glu | Glu | Asn | Pro | Glu | Ala | Ala | Asp | Ser |
| 23 | 1 | Буз | Бец | шуз | 5 | цуз | 7114 | Ora | Olu | 10 | 110 | 014 | | | 15 | |
| 20 | Gly | Glu | Pro | Gln 20 | Asn | Lys | Arg | Thr | Pro 25 | Asp | Leu | Pro | Glu | Glu 30 | Glu | Tyr |
| 30 | Val | Lys | Glu 35 | Glu | Ile | Gln | Glu | Asn 40 | Glu | Glu | Ala | Val | Lys 45 | Lys | Met | Leu |
| 35 | Val | Glu 50 | | Thr | Arg | Glu | Phe 55 | Glu | Glu | Val | Val | Val 60 | Asp | Glu | Ser | |
| 40 | (2) | INF | ORMA | SEQU | | CHA ENGT | RACT | ERIS | TICS | | lds | | | | | |
| 45 | | | (xi) | SEÇ | | OPOL | | | | EQ I | D NC |): 24 | 11: | | | |
| | Lys 1 | | a Met | Glu | Lys 5 | | Ser | Leu | Thr | Gln 10 | | Ser | Trp | Gln | Ser 15 | Let |
| 50 | Lys | s Asp | Arg | Tyr 20 | | Lys | His | Leu | Arg 25 | | Gln | Glu | His | Lys 30 | | Let |
| 55 | Lev | ı Gly | Asp 35 | | Pro | Val | Ser | Pro 40 | | Ser | Glr | Lys | Leu 45 | | : Arg | Lys |
| در | Ala | a Glu 50 | | a Asp | Pro | Glu | Ala 55 | | Asp | Ser | Gly | Glu 60 | ı Pro | Glr | ı Asn | Ly |
| 60 | Arg | - | r Pro |) Asp | Leu | Pro | | Glu | Glu | туг | - Val | | s Glu | Glu | ı Ile | G1: |

| | Glu | Asn | Glu | Glu | Ala 85 | Val | Lys | Lys | Met | Leu 90 | Val | Glu | Ala | Thr | Arg 95 | Glu |
|----|------------|------------|------------|-------------|----------------------|----------------------|---------------------|---------------------------------------|---------------------|-----------|-----------|------------|------------|------------|-----------|-----------|
| 5 | Phe | Glu | Glu | Val 100 | | Val | Asp | Glu | Ser 105 | | Pro | Asp | Phe | Glu 110 | _ | His |
| 10 | Ile | | | | | | | | | | | | | | | |
| 10 | | | | | | | | | | | | | | | | |
| 15 | (2) | | | SEQUI () | ENCE A) L B) T | CHAI ENGT YPE: | RACT H: 1 ami | NO: 2 ERIS' 48 a no a lin | rics mino cid | | ds | | | | | |
| 20 | | | (xi) | | | | | PTIO | | EQ I | D NO | : 24 | 2: | | | |
| 20 | Leu 1 | Pro | Ser | Tyr | Asp 5 | Glu | Ala | Glu | Arg | Thr 10 | Lys | Ala | Glu | Ala | Thr 15 | Ile |
| 25 | Pro | Leu | Val | Pro 20 | Gly | Arg | Asp | Glu | Asp 25 | Phe | Val | Gly | Arg | Asp 30 | Asp | Phe |
| | Asp | Asp | Ala 35 | Asp | Gln | Leu | Arg | Ile 40 | Gly | Asn | Asp | Gly | Ile 45 | Phe | Met | Leu |
| 30 | Thr | Phe 50 | Phe | Met | Ala | Phe | Leu 55 | Phe | Asn | Trp | Ile | Gly 60 | Phe | Phe | Leu | Ser |
| 35 | Phe 65 | Cys | Leu | Thr | Thr | Ser 70 | Ala | Ala | Gly | Arg | Tyr 75 | Gly | Ala | Ile | Ser | Gly 80 |
| 33 | Phe | Gly | Leu | Ser | Leu 85 | Ile | Lys | Trp | Ile | Leu 90 | Ile | Val | Arg | Phe | Ser 95 | Thr |
| 40 | Tyr | Phe | Pro | Gly 100 | Туг | Phe | Asp | Gly | Gln 105 | | Trp | Leu | Trp | Trp 110 | Val | Phe |
| | Leu | Val | Leu 115 | Gly | Phe | Leu | Leu | Phe 120 | Leu | Arg | Gly | Phe | Ile 125 | Asn | Тут | Ala |
| 45 | Lys | Val 130 | | Lys | Met | Pro | Glu 135 | | Phe | Ser | Asn | Leu 140 | | Arg | Thr | Arg |
| 50 | Val 145 | | Phe | Ile | | | | | | | | | | | | |
| | (2) | INF | ORMA | TION | FOR | . SEQ | ID | NO: | 243: | | | | | | | |
| 55 | | | (i) | | (A) I (B) 1 | LENGT | TH: 2 : am: | TERIS 24 ar ino a | mino acid | | ds | | | | | |
| 60 | | | (xi) | | | | | : lir [PTIC | | SEQ I | D NO |): 24 | 13 : | | | |

| | Ala 1 | Gly | Arg | Tyr | Gly 5 | Ala | Ile | Ser | Gly | Phe 10 | Gly | Leu | Ser | Leu | Ile 15 | Lys |
|----|-----------|-----------|-------------|-------------------|----------------------|------------------------|----------------------|--------------------------------------|--------------------|-----------|-----------|-----------|-----------|------------|-----------|-----------|
| 5 | Trp | Ile | Leu | Ile 20 | Val | Arg | Phe | Ser | | | | | | | | |
| 10 | (2) | | CAMAC | SEQUI () () | ENCE A) L B) T | CHAI ENGT: YPE : | RACTI H: 5 ami | ERIS 1 am no a | FICS ino a | | 5 | | | | | |
| 15 | | | (xi) | SEQU | | | | lin PTIO | | EQ II | ON C | : 24 | 4: | | | |
| | Met 1 | Lys | His | Leu | Ser 5 | Ala | Trp | Asn | Phe | Thr 10 | Lys | Leu | Thr | Phe | Leu 15 | Gln |
| 20 | Leu | Trp | Glu | Ile 20 | Phe | Glu | Gly | Ser | Val 25 | Glu | Asn | Cys | Gln | Thr 30 | Leu | Thr |
| 25 | Ser | Tyr | Ser 35 | Lys | Leu | Gln | Ile | Lys 40 | Tyr | Thr | Phe | Ser | Arg 45 | Gly | Ser | Thr |
| | Phe | Tyr 50 | Ile | | | | | | | | | | | | | |
| 30 | (2) | INF | ORMA! | rion | FOR | SEQ | ID I | NO: 2 | 245: | | | | | | | |
| 35 | | | (i) (xi) | (| A) L B) T D) T | ENGT YPE: 'OPOL | H: 2 ami OGY: | ERIS' 13 a no a lin PTIO | mino cid ear | aci | | : 24 | 5: | | | |
| 40 | Phe 1 | Ser | Ser | Asp | Phe 5 | Arg | Thr | Ser | Pro | Trp 10 | Glu | Ser | Arg | Arg | Val 15 | Glu |
| | Ser | Lys | Ala | Thr 20 | Ser | Ala | Arg | Cys | Gly 25 | Leu | Trp | Gly | Ser | Gly 30 | Pro | Arg |
| 45 | Arg | Arg | Pro 35 | Ala | Ser | Gly | Met | Phe 40 | Arg | Gly | Leu | Ser | Ser 45 | Trp | Leu | Gly |
| 50 | Leu | Gln 50 | Gln | Pro | Val | Ala | Gly 55 | Gly | Gly | Gln | Pro | Asn 60 | Gly | Asp | Ala | Pro |
| | Pro 65 | | Gln | Pro | Ser | Glu 70 | Thr | Val | Ala | Glu | Ser 75 | Ala | Glu | Glu | Glu | Leu 80 |
| 55 | Gln | Gln | Ala | Gly | Asp 85 | | Glu | Leu | Leu | His 90 | Gln | Ala | Lys | Asp | Phe 95 | Gly |
| | Asn | Тут | Leu | Phe 100 | | Phe | Ala | Ser | Ala 105 | Ala | Thr | Lys | Lys | Ile 110 | Thr | Glu |
| 60 | Ser | Val | Ala | Glu | Thr | Ala | Gln | Thr | Ile | Lys | Lys | Ser | Val | Glu | Glu | Gly |

| | | | 115 | | | | | 120 | | | | | 125 | | | |
|-----|------------|------------|----------------|------------|-------------------------|-----------------------------|------------------------|-------------------------|----------------------|------------|------------|------------|-------------|------------|------------|------------|
| 5 | Lys | Ile 130 | Asp | Gly | Ile | Ile | Asp 135 | Lys | Thr | Ile | Ile | Gly 140 | Asp | Phe | Gln | Lys |
| J | Glu 145 | Gln | Lys | Lys | Phe | Val 150 | Glu | Glu | Gln | His | Thr 155 | Lys | Lys | Ser | Glu | Ala 160 |
| 10 | Ala | Val | Pro | Pro | Trp 165 | Val | Asp | Thr | Asn | Asp 170 | Glu | Glu | Thr | Ile | Gln 175 | Gln |
| | Gln | Ile | Leu | Ala 180 | Leu | Ser | Ala | Asp | Lys 185 | Arg | Asn | Phe | Leu | Arg 190 | Asp | Pro |
| 15 | Pro | Ala | Gly 195 | Val | Gln | Phe | Asn | Phe 200 | Asp | Phe | Asp | Gln | Met 205 | Tyr | Pro | Val |
| 20 | Ala | Leu 210 | Val | Met | Leu | | | | | | | | | | | |
| | (2) | INF | ORMA' | rion | FOR | SEQ | ID I | NO: 1 | 246: | | | | | | | |
| 25 | | | (i) | (| A) L B) T | CHA ENGT YPE: OPOL | H: 4 ami | 9 am .no a | ino cid | | s | | | | | |
| 30 | | | | SEQ | | | | | | | | | | 17-1 | Dho | (1) |
| | Met 1 | Arg | Pne | Ala | ьeu 5 | vai | Pro | ьys | Leu | 10 | ьys | Giu | GIU | vai | 15 | 111 |
| 35 | Arg | Asn | Tyr | Phe 20 | Tyr | Arg | Val | Ser | Leu 25 | Ile | Lys | Gln | Ser | Ala 30 | Gln | Leu |
| | Thr | Ala | Leu 35 | Ala | Ala | Gln | Gln | Gln 40 | Ala | Ala | Gly | Lys | Gly 45 | Gly | Glu | Glu |
| 40 | Gln | | | | | | | | | | | | | | | |
| 45 | (2) | INF | ORMA | TION | FOR | SEQ |) ID | NO: | 247: | | | | | | | |
| 50 | | | , ", ", | | (A) I (B) : (D) : | LENGT TYPE TOPOI | TH: ' : am: LOGY | 76 ar ino a : lir | mino acid near | acio | | D: 24 | 17 : | | | |
| ~ ~ | Ser 1 | | Ser | Pro | Gly 5 | | Ser | Glu | Phe | • Val | | Asp | Ala | Phe | Asp 15 | |
| 55 | Cys | Asr | ı Lev | Asn 20 | | Glu | ı Asp | Lev | Arg 25 | | Glı | ı Met | : Glu | Glr 30 | | ı Va |
| 60 | Leu | . Asp |) Ly s | E Lys | Glr | ı Glu | ı Glı | Thi | | a Val | Le | ı Glu | a Glu 45 | | Ser | `Al |

| | Asp | Trp 50 | Glu | Lys | Glu | Leu | Gln 55 | Gln | Glu | Leu | Gln | Glu 60 | Tyr | Glu | Val | Val |
|-----|-----------|-----------|-----------|-----------|----------------------|----------------------|---------------------|-------------------------------------|-------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----|
| 5 | Thr 65 | Glu | Ser | Glu | Lys | Arg 70 | Asp | Glu | Asn | Trp | Asp 75 | Lys | | | | |
| 10 | (2) | INF | ORMA! | rion | FOR | SEQ | I DI | NO: 2 | 248: | | | | | | | |
| 15 | | | | (| A) L B) T D) T | ENGT YPE: OPOL | H: 6 ami OGY: | ERIS 2 am no a lin PTIO | ino cid ear | acid | | : 24 | B: | | | |
| 20 | Ser 1 | Pro | Trp | Glu | Ser 5 | Arg | Arg | Val | Glu | Ser 10 | Lys | Ala | Thr | Ser | Ala 15 | Arg |
| 20 | Cys | Gly | Leu | Trp 20 | Gly | Ser | Gly | Pro | Arg 25 | Arg | Arg | Pro | Ala | Ser 30 | Gly | Met |
| 25 | Phe | Arg | Gly 35 | Leu | Ser | Ser | Trp | Leu 40 | Gly | Leu | Gln | Gln | Pro 45 | Val | Ala | Gly |
| | Gly | Gly 50 | | Pro | Asn | Gly | Asp 55 | Ala | Pro | Pro | Glu | Gln 60 | Pro | Ser | | |
| 30 | | | | | | | | | | | | | | | | |
| | (2) | INF | | | | | | NO: : | | | | | | | | |
| 35 | | | | ~ (| A) L B) T D) T | ENGT YPE: OPOL | H: 6 ami OGY: | ERIS 5 am no a lin PTIO | ino cid ear | acid | | : 24 | 9: | | | |
| 40 | Pro | | Ala | Gly | Gly 5 | Gly | Gln | Pro | Asn | Gly 10 | Asp | Ala | Pro | Pro | Glu 15 | Gln |
| 4.5 | Pro | Ser | Glu | Thr 20 | Val | Ala | Glu | Ser | Ala 25 | Glu | Glu | Glu | Leu | Gln 30 | Gln | Ala |
| 45 | Gly | Asp | Gln 35 | | Leu | Leu | His | Gln 40 | Ala | Lys | Asp | Phe | Gly 45 | Asn | Tyr | Leu |
| 50 | Phe | Asn 50 | | Ala | Ser | Ala | Ala 55 | | Lys | Lys | Ile | Thr 60 | Glu | Ser | Val | Ala |
| | Glu 65 | | | | | | | | | | | | | | | |
| 55 | | | | | | | | | | | | | | | | |
| | (2) | INF | | | | | | NO: | | | | | | | | |
| 60 | | | (1) | _ | | | | TERIS 72 ar | | | ls | | | | | |

| | | | (xi) | (| D) T | OPOL | OGY: | no a lin PTIO | | EQ II | ON C | : 25 | 0: | | | |
|-----|-----------|-----------|-----------|-----------|----------------------|----------------------|---------------------|---------------------|----------------------|-----------|------|-----------|-----------|-----------|-----------|-----|
| 5 | Phe 1 | Gln | Lys | Glu | Gln 5 | Lys | Lys | Phe | Val | Glu 10 | Glu | Gln | His | Thr | Lys 15 | Lys |
| 10 | Ser | Glu | Ala | Ala 20 | Val | Pro | Pro | Trp | Val 25 | Asp | Thr | Asn | Asp | Glu 30 | Glu | Thr |
| 10 | Ile | Gln | Gln 35 | Gln | Ile | Leu | Ala | Leu 40 | Ser | Ala | Asp | Lys | Arg 45 | Asn | Phe | Leu |
| 15 | Arg | Asp 50 | Pro | Pro | Ala | Gly | Val 55 | Gln | Phe | Asn | Phe | Asp 60 | Phe | Asp | Gln | Met |
| | Туr 65 | Pro | Val | Ala | Leu | Val 70 | Met | Leu | | | | | | | | |
| 20 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA' | rion | FOR | SEQ | ID I | NO: | 251: | | | | | | | |
| 25 | | | | (| A) L B) T D) T | ENGT YPE: OPOL | H: 2 ami OGY: | 8 am no a lir | | acid | | : 25 | 1: | | | |
| 30 | Pro 1 | Phe | Ile | Cys | Val 5 | Ala | Arg | Asn | Pro | Val 10 | Ser | Arg | Asn | Phe | Ser 15 | Ser |
| 35 | Pro | Ile | Leu | Ala 20 | Arg | Lys | Leu | Cys | Glu 25 | Gly | Ala | Ala | | | | |
| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 252: | | | | | | | |
| 40 | | | (i) | | (A) I | ENGT | TH: 3 | | TICS mino acid | | ls | | | | | |
| 4.5 | | | (xi) | | | | | : lir | near N: S | SEQ] | D NO | o: 25 | 52: | | | |
| 45 | Lys 1 | | ı Asp | Pro | Ala 5 | | Thr | Val | Туг | Ser 10 | | · Val | . Glu | lle | Pro | |
| 50 | Lys | Met | Glu | Asr 20 | | His | Ser | Leu | Leu 25 | | Met | Pro | Asp | Thr 30 | | Ar |
| | Leu | l | | | | | | | | | | | | | | |
| 55 | | | | | | | | | | | | | | | | |
| | (2) | IN | FORM | OITA | 1 FOF | R SEÇ | Q ID | NO: | 253 : | : | | | | | | |
| 60 | | | (i) | SEQ | | | | | STIC: amin | | ids | | | | | |

| | | | (xi) | C | D) T | OPOL | OGY: | lin | ear | EQ II | O M C | : 253 | 3: | | | |
|------------|------------|------------|------------|------------|-------------------------|--------------------------|---------------------|-------------------------|----------------------|------------|--------------|------------|--------------|------------|------------|------------|
| 5 | Ala 1 | Ser | Ala | Val | Leu 5 | Leu | Asp | Leu | Pro | Asn 10 | Ser | Gly | Gly | Glu | Ala 15 | Gln |
| 10 | Ala | Lys | Lys | Leu 20 | Gly | Asn | Asn | Cys | Val 25 | Phe | Ala | Pro | Ala | Asp 30 | Val | Thr |
| 10 | Ser | Glu | Lys 35 | Asp | Val | Gln | Thr | Ala 40 | Leu | Ala | Leu | Ala | Lys 45 | Gly | Lys | Phe |
| 15 | Gly | Arg 50 | Val | Asp | Val | Ala | Val 55 | Asn | Cys | Ala | Gly | Ile 60 | Ala | Val | Ala | Ser |
| | Lys 65 | Thr | Tyr | Asn | Leu | Lys 70 | Lys | Gly | Gln | Thr | His 75 | Thr | Leu | Glu | Asp | Phe 80 |
| 20 | Gln | Arg | Val | Leu | Asp 85 | Val | Asn | Leu | Met | Gly 90 | Thr | Phe | Asn | Val | Ile 95 | Arg |
| 25 | Leu | Val | Ala | Gly 100 | Glu | Met | Gly | Gln | Asn 105 | Glu | Pro | Asp | Gln | Gly 110 | Gly | Gln |
| 2 3 | Arg | Gly | Val 115 | Ile | Ile | Asn | Thr | Ala 120 | Ser | Val | Ala | Ala | Phe 125 | Glu | Gly | Gln |
| 30 | Val | Gly 130 | Gln | Ala | Ala | Tyr | Ser 135 | Ala | Ser | Lys | Gly | Gly 140 | Ile | Val | Gly | Met |
| | Thr 145 | Leu | Pro | Ile | Ala | Arg 150 | Asp | Leu | Ala | Pro | Ile 155 | Gly | Ile | Arg | Val | Met 160 |
| 35 | Thr | Ile | Ala | Pro | Gly 165 | Leu | Phe | Gly | Thr | Pro 170 | Leu | Leu | Thr | Ser | Leu 175 | Pro |
| 40 | Glu | Lys | Val | Cys 180 | Asn | Phe | Leu | Ala | Ser 185 | Gln | Val | Pro | Phe | Pro 190 | Ser | Arg |
| 70 | Leu | Gly | Asp 195 | Pro | Ala | Glu | Tyr | Ala 200 | His | Leu | Val | Gln | Ala 205 | Ile | Ile | Glu |
| 45 | Asn | Pro 210 | | Leu | Asn | Gly | Glu 2 1 5 | Val | Ile | Arg | Leu | Asp 220 | Gly | Ala | Ile | Arg |
| | Met 225 | | Pro | | | | | | | | | | | | | |
| 50 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 254: | | | | | | | |
| 55 | | | | | (A) I (B) : (D) : | LENGT TYPE : TOPOI | RACT TH: 2 tami | 29 am ino a : lir | mino acid near | acio | is ID NO |): 25 | 5 4 : | | | |
| 60 | Ser | . Val | | | _ | | | | | | | | | Tyr | Ser | Ala |

345

| | 1 | | | 5 | | | | | 10 | | | | | 15 | |
|----|----------|-------------|-------------|----------------------------|----------------------|----------------------|-----------------------|--------------------|-----------|-------|---------------|-----------|-----------|-----------|-----|
| 5 | Ser | Lys Gl | y Gly 20 | Ile ' | Val | Gly | Met | Thr 25 | Leu | Pro | Ile | Ala | | | |
| | (2) | INFORM | ATION | FOR : | SEQ | ID N | 10: 2 | 255 : | | | | | | | |
| 10 | | | (| A) LE B) TY D) TO | NGTI PE: POLC | d: 6 ami DGY: | l am no a lin | ino cid ear | acid | | : 25 | 5: | | | |
| 15 | Ala 1 | Arg Ar | g Ser | Gly i | Ala | Glu | Leu | Ala | Trp 10 | Asp | Tyr | Leu | Cys | Arg 15 | Trp |
| 20 | Ala | Gln Ly | s His 20 | Lys i | Asn | Trp | Arg | Phe 25 | Gln | Lys | Thr | Arg | Gln 30 | Thr | Trp |
| | Leu | Leu Le 3 | | Met ' | Tyr | Asp | Ser 40 | Asp | Lys | Val | Pro | Asp 45 | Glu | His | Phe |
| 25 | Ser | Thr Le | u Leu | Ala ' | Tyr | Leu 55 | Glu | Gly | Leu | Gln | Gly 60 | Arg | | | |
| 30 | (2) | | SEQU (| ENCE A) LE B) TY | CHAF NGTI 'PE: | RACTI H: 2 ami | ERIS' 2 am no a | rics ino cid | | s | | | | | |
| 35 | | (xi |) SEQ | D) TC UENCE | | | | | EQ I | D NIO | : 25 | 6: | | | |
| | His 1 | Pro Il | e Glu | Trp . | Ala | Ile | Asn | Ala | Ala 10 | Thr | Leu | Ser | Gln | Phe 15 | Туr |
| 40 | Ile | Asn Ly | s Leu 20 | Cys : | Phe | | | | | | | | | | |
| 45 | (2) | INFORM | NOITA | FOR | SEQ | ID 1 | 10: 3 | 257: | | | | | | | |
| 50 | | | (| (A) LE (B) TY (D) TO | ENGTI PE: POL | H: 2 ami OGY: | 2 am no a lin | ino cid ear | acid | |): 2 5 | 7: | | | |
| 55 | 1 | Trp Il | | 5 Ile | _ | Leu | Thr | Leu | Met 10 | Gln | Asn | Ala | Gln | Leu 15 | Ser |

BNSDOCID: <WO___9842738A1_IA>

| | (2) INFORMATION FOR SEQ ID NO: 258: |
|----|---|
| 5 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 258: |
| 10 | Lys Val Ser Tyr Leu Arg Pro Leu Asp Phe Glu Glu Ala Arg Glu Leu 1 5 10 15 |
| | Phe Leu Leu Gly Gln His Tyr Val Phe 20 25 |
| 15 | |
| | (2) INFORMATION FOR SEQ ID NO: 259: |
| 20 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 259: |
| 25 | Met Glu Arg Arg Cys Lys Met His Lys Arg Xaa Ile Ala Met Leu Glu 1 5 10 15 |
| 30 | Pro Leu Thr Val Asp Leu Asn Pro Gln 20 25 |
| | (2) INFORMATION FOR SEQ ID NO: 260: |
| 35 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 260: Ser His Ile Val Lys Lys Ile Asn Asn Leu Asn Lys Ser Ala Leu Lys |
| | 1 5 10 15 15 15 15 15 15 15 15 15 15 15 15 15 |
| 45 | Tyr Tyr Gln Leu Phe Leu Asp 20 |
| 50 | (2) INFORMATION FOR SEQ ID NO: 261: |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 64 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear |
| 55 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 261: |
| | Phe Thr His Leu Ser Thr Cys Leu Leu Ser Leu Leu Leu Val Arg Met 1 5 10 15 |
| 60 | Cor Cly Dho Lou Lou Lau Ala Arg Ala Car Dro Cor Ile Cyc Ala Leu |

| | 20 | | 25 | | 30 |
|----|---|--|----------------------|-----------------|-------------------|
| _ | Asp Ser Ser Cys Phe | e Val Gln Glu 40 | | Ser Tyr S 45 | Ser Ser Ser |
| 5 | Cys Phe Leu His Glr 50 | n His Phe Pro 55 | Ser Leu Leu | Asp His I | Leu Cys Gln |
| 10 | | | | | |
| 15 | (A) | R SEQ ID NO: E CHARACTERI LENGTH: 23 a TYPE: amino | STICS: | | |
| 20 | • | TOPOLOGY: li CE DESCRIPTI | near ON: SEQ ID N | D: 26 2: | |
| | Phe Leu Leu Leu Ala | | Pro Ser Ile | e Cys Ala 1 | Leu Asp Ser 15 |
| 25 | Ser Cys Phe Val Glr 20 | n Glu Tyr | | | |
| 30 | (2) INFORMATION FOR | R SEQ ID NO: | 263: | | |
| 35 | (A) (B) (D) | E CHARACTERI LENGTH: 53 a TYPE: amino TOPOLOGY: li CE DESCRIPTI | mino acids acid | O: 263: | |
| 40 | _ | 5 | 10 | | 15 |
| | Phe Gly Met Ile Gly 20 | y Leu Leu Th | r Phe Ile Ar 25 | g Ala Ala | Glu Thr Asp 30 |
| 45 | Pro Gly Met Val His | | u Gly Ser As 0 | p Leu Thr 45 | Thr Leu Gly |
| | Leu Asn Leu Asn Se 50 | r | | | |
| 50 | | | | | |
| | (2) INFORMATION FO | R SEQ ID NO: | 264: | | |
| 55 | (A) (B) (D) | E CHARACTERI LENGTH: 41 a TYPE: amino TOPOLOGY: 1: ICE DESCRIPTI | amino acids acid | IO: 264: | |
| 60 | Glu Asp Leu Leu Ph | e Tvr Leu Tv | r Tyr Met As | n Gly Gly | Asp Val Le |

| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
|----|----------|-----------|-----------|------------|-------------------------|-------------------------|-----------------------|---------------------------------------|---------------------|-----------|-------|-----------|-----------|-----------|-----------|-----|
| _ | Gln | Leu | Leu | Ala 20 | Ala | Val | Glu | Leu | Phe 25 | Asn | Arg | Asp | Trp | Arg 30 | Tyr | His |
| 5 | Lys | Glu | Glu 35 | Arg | Val | Trp | Ile | Thr 40 | Arg | | | | | | | |
| 10 | (2) | INFO | ORMAT | NOI | FOR | SEQ | ID N | ю: 2 | 65: | | | | | | | |
| 15 | | | | () (1 | A) LI B) T D) T | ENGTI YPE : OPOLA | H: 24 amii DGY: | ERIST 4 amm no ac line PTION | ino a cid ear | acid | | : 26! | 5: | | | |
| 20 | Val 1 | His | Leu | Ala | Leu 5 | Gly | Ser | Asp | Leu | Thr 10 | Thr | Leu | Gly | Leu | Asn 15 | Leu |
| | Asn | Ser | Pro | Glu 20 | Asn | Leu | Tyr | Pro | | | | | | | | |
| 25 | | | | | | | | | | | | | | | | |
| | (2) | INF | CAMAC | rion | FOR | SEQ | ID 1 | N O: 2 | 266 : | | | | | | | |
| 30 | | | | - (, (, | A) L B) T D) T | ENGT YPE : OPOL | H: 4 ami OGY: | ERIS 1 am no a lin PTIO | ino cid ear | acid | | : 26 | 6: | | | |
| 35 | His 1 | | Glu | Asp | Phe 5 | Pro | Ala | Leu | Pro | Gly 10 | Ser | | | | | |
| 40 | (2) | INF | ORMA | TION | FOR | SEQ | ID ! | NO: 2 | 267: | | | | | | | |
| 45 | | | | (| (A) L (B) T (D) T | ENGT YPE: OPOL | H: 7 ami OGY: | ERIS' '5 am no a lin PTIO | ino cid ear | ació | | o: 26 | 57 : | | | |
| 50 | Gly 1 | | Ile | Ile | Asp 5 | Thr | Ser | Leu | Thr | Arg 10 | | Pro | Leu | Val | Ile 15 | Glu |
| JU | Leu | Gly | Gln | Lys 20 | | Val | Ile | Pro | Gly 25 | Leu | Glu | Gln | . Ser | Leu 30 | Leu | Asp |
| 55 | Met | : Cys | 35 | | Glu | Lys | Arg | Arg 40 | Ala | Ile | · Ile | Pro | Ser 45 | His | Leu | Ala |
| | Туг | Gly 50 | | Arg | Gly | Phe | Pro 55 | | Ser | Val | . Pro | Ala 60 | | Ala | Val | Val |
| 60 | Glr | ı Tvr | Asc | Val | Glu | Leu | Ile | Ala | Leu | . Il∈ | Arq | ı | | | | |

349

65 70 75 5 (2) INFORMATION FOR SEQ ID NO: 268: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 10 (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 268: Ile His Tyr Thr Gly Ser Leu Val Asp Gly Arg Ile Ile Asp Thr Ser 15 20 (2) INFORMATION FOR SEQ ID NO: 269: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 269: Cys Glu Ser Pro Glu Ser Pro Ala Gln Pro Ser Gly Ser Ser Leu Pro 30 Ala Trp Tyr His 35 (2) INFORMATION FOR SEQ ID NO: 270: (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 95 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 270: 45 Glu Glu Ala Gly Ala Gly Arg Arg Cys Ser His Gly Gly Ala Arg Pro Ala Gly Leu Gly Asn Glu Gly Leu Gly Leu Gly Gly Asp Pro Asp His 50 Thr Asp Thr Gly Ser Arg Ser Lys Gln Arg Ile Asn Asn Trp Lys Glu Ser Lys His Lys Val Ile Met Ala Ser Ala Ser Ala Arg Gly Asn Gln 55

Asp Lys Asp Ala His Phe Pro Pro Pro Ser Lys Gln Ser Leu Leu Phe

Cys Pro Lys Ser Lys Leu His Ile His Arg Ala Glu Ile Ser Lys

75

350

90

| 5 . | (2) INFORMATION FOR SEQ ID NO: 271: |
|-----------|--|
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 271: |
| 15 | Ser Lys Gln Arg Ile Asn Asn Trp Lys Glu Ser Lys His Lys Val Ile 1 5 10 15 Met Ala Ser Ala Ser Ala Arg |
| 20 | 20 (2) INFORMATION FOR SEQ ID NO: 272: |
| 25 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 272: |
| 30 | Leu Phe His Trp Ala Cys Leu Asn Glu Arg Ala Ala Gln Leu Pro Arg 1 5 10 15 |
| 35 | Asn Thr Ala Xaa Ala Gly Tyr Gln Cys Pro Ser Cys Asn Gly Pro Ser 20 25 30 |
| 40 | (2) INFORMATION FOR SEQ ID NO: 273: |
| 45 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 185 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 273: |
| 50 | Phe Tyr Ile Tyr Tyr Arg Pro Thr Asp Ser Asp Asn Asp Ser Asp Tyr 1 5 10 15 |
| 50 | Lys Lys Asp Met Val Glu Gly Asp Lys Tyr Trp His Ser Ile Ser His 20 25 30 |
| 55 | Leu Gln Pro Glu Thr Ser Tyr Asp Ile Lys Met Gln Cys Phe Asn Glu 35 40 45 |
| | Gly Gly Glu Ser Glu Phe Ser Asn Val Met Ile Cys Glu Thr Lys Ala 50 55 60 |
| 60 | Arg Lys Ser Ser Gly Gln Pro Gly Arg Leu Pro Pro Pro Thr Leu Ala |

| | 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
|----|---------------------|------------|------------|------------|-------------------------|--------------------------|------------------------|-------------------------|----------------------|------------|------------|------------|------------|------------|------------|------------|--|
| _ | Pro | Pro | Gln | Pro | Pro 85 | Leu | Pro | Glu | Thr | Ile 90 | Glu | Arg | Pro | Val | G1y 95 | Thr | |
| 5 | Gly | Ala | Met | Val | Ala | Arg | Ser | Ser | Asp 105 | Leu | Pro | Tyr | Leu | Ile 110 | Val | Gly | |
| 10 | Val | Val | Leu 115 | Gly | Ser | Ile | Val | Leu 120 | Ile | Ile | Val | Thr | Phe 125 | Ile | Pro | Phe | |
| | Cys | Leu 130 | Trp | Arg | Ala | Trp | Ser 135 | Lys | Gln | Lys | His | Thr 140 | Thr | Asp | Leu | Gly | |
| 15 | Phe 1 4 5 | Pro | Arg | Ser | Ala | Leu 150 | Pro | Pro | Ser | Cys | Pro 155 | Tyr | Thr | Met | Val | Pro 160 | |
| 20 | Leu | Gly | Gly | Leu | Pro 165 | Gly | His | Gln | Ala | Val 170 | Asp | Ser | Pro | Thr | Ser 175 | Val | |
| 20 | Ala | Ser | Val | Asp 180 | Gly | Pro | Val | Leu | Met 185 | | | | | | | | |
| 25 | (2) | TATE | ODMA | TION | FOR | SEO | TD : | NO· ΄ | 274 • | | | | | | | | |
| | (2) | 1141 | | SEQU | ENCE | СНА | RACT | | TICS | | ls | | | | | | |
| 30 | | | (xi) | (| B) T | YPE : OPOL | ami OGY: | no a | cid ear | | |): 27 | 4: | | | | |
| 35 | Tyr 1 | | Tyr | Туr | Arg 5 | Pro | Thr | Asp | Ser | Asp 10 | Asn | Asp | Ser | Asp | Tyr 15 | Lys | |
| | Lys | Asp | Met | Val 20 | | Gly | Asp | Lys | Тут 25 | | His | Ser | Ile | Ser 30 | His | Leu | |
| 40 | Gln | Pro | Glu 35 | Thr | Ser | Tyr | Asp | Ile 40 | | Met | Gln | Cys | Phe 45 | Asn | Glu | Gly | |
| 45 | Gly | Glu 50 | | Glu | Phe | Ser | Asn 55 | | Met | Ile | Cys | Glu 60 | | Lys | Ala | Arg | |
| 73 | Lys 65 | Ser | | | | | | | | | | | | | | | |
| 50 | (2) | INF | ORMA | MOIT | I FOR | SEQ |) ID | NO: | 275: | | | | | | | | |
| 55 | | | | | (A) 1 (B) 1 (D) 1 | LENG' I'YPE I'OPO! | TH: : : am: LOGY | 30 ar ino a : lin | mino acid near | acio | | D: 27 | 75: | | | | |
| 60 | Asr 1 | ı Val | l Arg | g Ala | Leu 5 | | ı His | arç | , Met | Pro | | ı Pro | Pro | Lys | : Ile | Asn | |

| | Thr | Ala | Lys | Phe 20 | Asn | Asn | Asn | Lys | Arg 25 | Lys | Asn | Leu | Ser | Leu 30 | | |
|----|------------|------------|---------------|------------|----------------------|-----------------------|---------------------|---------------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMAT | NOI | FOR | SEQ | ID 1 | NO: 2 | 276: | | | | | | | |
| 10 | | | (i) ; (xi) | (| A) L B) T D) T | ENGT YPE : OPOL | H: 1 ami OGY: | 85 a no a lin | cid ear | aci | | : 27 | 6: | | | |
| 15 | Asn 1 | Thr | Asn | Gln | Arg 5 | Glu | Ala | Leu | Gln | Туг 10 | Ala | Lys | Asn | Phe | Gln 15 | Pro |
| 20 | Phe | Ala | Leu | Asn 20 | His | Gln | Lys | Asp | Ile 25 | Gln | Val | Leu | Met | Gly 30 | Ser | Leu |
| 20 | Val | Tyr | Leu 35 | Arg | Gln | Gly | Ile | Glu 40 | Asn | Ser | Pro | Tyr | Val 45 | His | Leu | Leu |
| 25 | Asp | Ala 50 | Asn | Gln | Trp | Ala | Asp 55 | Ile | Cys | Asp | Ile | Phe 60 | Thr | Arg | Asp | Ala |
| | Cys 65 | Ala | Leu | Leu | Gly | Leu 70 | Ser | Val | Glu | Ser | Pro 75 | Leu | Ser | Val | Ser | Phe 80 |
| 30 | Ser | Ala | Gly | Cys | Val 85 | Ala | Leu | Pro | Ala | Leu 90 | Ile | Asn | Ile | Lys | Ala 95 | Val |
| 35 | Ile | Glu | Gln | Arg 100 | Gln | Cys | Thr | Gly | Val 105 | Trp | Asn | Gln | Lys | Asp 110 | Glu | Leu |
| 20 | Pro | Ile | Glu 115 | Val | Asp | Leu | Gly | Lys 120 | Lys | Cys | Trp | Tyr | His 125 | Ser | Ile | Phe |
| 40 | Ala | Суs 130 | | Ile | Leu | Arg | Gln 135 | Gln | Thr | Thr | Asp | Asn 140 | Asn | Pro | Pro | Met |
| | Lys 145 | Leu | Val | Cys | Gly | His 150 | | Ile | Ser | Arg | Asp 155 | Ala | Leu | Asn | Lys | Met 160 |
| 45 | Phe | Asn | Gly | Ser | Lys 165 | Leu | Lys | Cys | Pro | Туг 170 | | Pro | Met | Glu | Gln 175 | Ser |
| 50 | Pro | Gly | Asp | Ala 180 | _ | Gln | Ile | Phe | Phe 185 | | | | | | | |
| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 277: | | | | | | | |
| 55 | | | (i) | - | (A) I (B) T | ENGT | TH: 6 | 55 an ino a | cid | : ació | ls | | | | | |
| 60 | | | (xi) | | | | | PTIC | | EQ I | D NC |): 27 | 77: | | | |

| | Ser 1 | Tyr | Leu | Ser | Ala 5 | Cys | Phe | Ala | Gly | Cys 10 | Asn | Ser | Thr | Asn | Leu 15 | Thr |
|----|-----------|-----------|-----------|-----------|------------------------------|------------------------------|-----------------------------|------------------------------|---------------------------|-----------|-----------|---------------|-----------|-----------|-----------|-----------|
| 5 | Gly | Cys | Ala | Cys 20 | Leu | Thr | Thr | Val | Pro 25 | Ala | Glu | Asn | Ala | Thr 30 | Val | Val |
| | Pro | Gly | Lys 35 | Cys | Pro | Ser | Pro | Gly 40 | Cys | Gln | Glu | Ala | Phe 45 | Leu | Thr | Phe |
| 10 | Leu | Cys 50 | Val | Met | Cys | Ile | Cys 55 | Ser | Leu | Ile | Gly | Ala 60 | Met | Ala | Arg | His |
| 15 | Pro 65 | | | | | | | | | | | | | | | |
| 20 | (2) | INF | (i) | (| ENCE A) L B) T D) T | CHAI ENGT YPE: OPOL | RACT H: 8 ami OGY: | ERIS' 4 am no a lin | rics ino cid ear | acid | | : 27 | 8: | | | |
| 25 | Pro 1 | Ser | Val | Ile | Ile 5 | Leu | Ile | Arg | Thr | Val | Ser | Pro | Glu | Leu | Lys 15 | Ser |
| 30 | Tyr | Ala | Leu | Gly 20 | Val | Leu | Phe | Leu | Leu 25 | Leu | Arg | Leu | Leu | Gly 30 | Phe | Ile |
| | | | 35 | Leu | | | | 40 | | | | | 45 | | | |
| 35 | Trp | Ser 50 | | Phe | Cys | Gly | Glu 55 | Gln | Gly | Ala | Cys | Val 60 | Leu | Tyr | Asp | Asn |
| 40 | 65 | | - | Arg | Tyr | Leu 70 | Tyr | Val | Ser | Ile | Ala 75 | Ile | Ala | Leu | Lys | Ser 80 |
| 45 | (2) | INF | 'ORMA | MOIT | FOR | SEQ | ID | NO: | 279: | | | | | | | |
| 50 | | | ,-, | (| (A) I (B) T (D) T | ENGT TYPE : TOPOL | H: 1 ami | l82 a ino a : lir | mind acid near | aci | |): 2 7 | '9 : | | | |
| 55 | Gln 1 | | Leu | ı Phe | Thr 5 | | Phe | Val | Arg | Val | | Val | Pro | Thr | Val 15 | Asp |
| | Leu | ı Asp | Ala | Gln 20 | | Arg | Ala | Arg | Ala 25 | | Leu | Cys | Xaa | Xaa 30 | | Asn |
| 60 | Trp | Arg | Tyr | Lys | Asn | Leu | Gly | Asn | Leu | Pro | His | . Val | Glr | Leu | Leu | Pro |

| | | | 35 | | | | | 40 | | | | | 45 | | | |
|----|------------|------------|------------|------------|-----------------------|-----------------------|---------------------|-----------------------------|-------------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Glu | Phe 50 | Ser | Thr | Ala | Asn | Ala 55 | Gly | Leu | Leu | Tyr | Asp 60 | Phe | Gln | Leu | Ile |
| 3 | Asn 65 | Val | Glu | Asp | Phe | Gln 70 | Gly | Val | Gly | Glu | Ser 75 | Glu | Pro | Asn | Pro | Туr 80 |
| 10 | Phe | Tyr | Gln | Asn | Leu 85 | Gly | Glu | Ala | Glu | Tyr 90 | Val | Val | Ala | Leu | Phe 95 | Met |
| | Tyr | Met | Cys | Leu 100 | Leu | Gly | Tyr | Pro | Ala 105 | Asp | Lys | Ile | Ser | Ile 110 | Leu | Thr |
| 15 | Thr | Tyr | Asn 115 | Gly | Gln | Lys | His | Leu 120 | Ile | Arg | Asp | Ile | Ile 125 | Asn | Arg | Arg |
| 20 | Cys | Gly 130 | Asn | Asn | Pro | Leu | Ile 135 | Gly | Arg | Pro | Asn | Lys 140 | Val | Thr | Thr | Val |
| 20 | Asp 145 | Arg | Phe | Gln | Gly | Gln 150 | Gln | Asn | Asp | Tyr | Ile 155 | Leu | Leu | Ser | Leu | Val 160 |
| 25 | Arg | Thr | Arg | Ala | Val 165 | Gly | His | Leu | Arg | Asp 170 | Val | Arg | Arg | Leu | Val 175 | Val |
| | Ala | Met | Ser | Arg 180 | Ala | Arg | | | | | | | | | | |
| 30 | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA' | rion | FOR | SEQ | ID I | NO: | 280: | | | | | | | |
| 35 | | | | (| (A) I (B) I (D) | ENGI YPE : OPOL | H: 7 ami OGY: | ERIS 7 am no a lin | ino cid ear | ació | |): 28 | 0: | | | |
| 40 | Leu 1 | | Lys | Glu | Ala 5 | | Ile | Ile | Ala | Met 10 | | Cys | Thr | His | Ala 15 | Alā |
| 15 | Leu | Lys | Arg | His 20 | | Leu | Val | Lys | Leu 25 | | Phe | Lys | Tyr | Asp 30 | | Ile |
| 45 | Leu | Met | Glu 35 | | Ala | Ala | Gln | . Ile 40 | | Glu | Ile | Glu | Thr 45 | | Ile | Pro |
| 50 | Leu | Leu 50 | | Gln | . Asn | Pro | Gln 55 | Asp | Gly | Phe | e Ser | Arg | | Lys | Arg | Tr |
| | 11e 65 | | : Ile | : Gly | Asp | His | | Gln | Leu | Pro | Pro 75 | | Ile | ! | | |
| 55 | | | | | | | | | | | | | | | | |
| | (2) | INF | FORMA | MOITA | 1 FOF | SEÇ | DI | NO: | 281: | | | | | | | |
| 60 | | | (i) | - | | | | reris | | | ids | | | | | |

| | | | (xi) | (| D) T | OPOL | OGY: | no a lin PTIO | ear | EQ II | ои с | : 28: | 1: | | | |
|----|-----------|-----------|------------|------------|----------------------|----------------------|---------------------|--------------------------------------|-------------------|-----------|-----------|-----------|------------|------------|-----------|-----------|
| 5 | Asp | Thr | Tyr | Pro | Asn 5 | Glu | Glu | Lys | Gln | Gln 10 | Glu | Arg | Val | Phe | Pro 15 | Xaa |
| 10 | Xaa | Ser | Ala | Met 20 | Val | Asn | Asn | Gly | Ser 25 | Leu | Ser | Tyr | Asp | His 30 | Glu | Arg |
| | Asp | Gly | Arg 35 | Pro | Thr | Glu | Leu | Gly 40 | Gly | Cys | Xaa | Ala | Ile 45 | Val | Arg | Asn |
| 15 | Leu | His 50 | Tyr | Asp | Thr | Phe | Leu 55 | Val | Ile | Arg | Tyr | Val 60 | Lys | Arg | His | Leu |
| | Thr 65 | Ile | Met | Met | Asp | Ile 70 | Asp | Gly | Lys | His | Glu 75 | Trp | Arg | Asp | Cys | Ile 80 |
| 20 | Glu | Val | Pro | Gly | Val 85 | Arg | Leu | Pro | Arg | Gly 90 | Tyr | Tyr | Phe | Gly | Thr 95 | Ser |
| 25 | Ser | Ile | Thr | Gly 100 | Asp | Leu | Ser | Asp | Asn 105 | His | Asp | Val | Ile | Ser 110 | Leu | Lys |
| 23 | Leu | Phe | Glu 115 | Leu | Thr | Val | Glu | Arg 120 | Thr | Pro | Glu | Glu | Glu 125 | | | |
| 30 | (2) | INF | ORMA' | rion | FOR | SEQ | ID I | NO: 2 | 282: | | | | | | | |
| 35 | | | | (| A) L B) T D) T | ENGT YPE: OPOL | H: 8 ami OGY: | ERIS' 5 am no a lin PTIO | ino cid ear | acid | | : 28 | 2: | | | |
| 40 | Leu 1 | Lys | Arg | Glu | His 5 | Ser | Leu | Ser | Lys | Pro 10 | Tyr | Gln | Gly | Val | Gly 15 | Thr |
| | Gly | Ser | Ser | Ser 20 | Leu | Trp | Asn | Leu | Met 25 | Gly | Asn | Ala | Met | Val 30 | Met | Thr |
| 45 | Gln | Tyr | Ile 35 | Arg | Leu | Thr | Pro | Asp 40 | Met | Gln | Ser | Lys | Gln 45 | Gly | Ala | Leu |
| 50 | Trp | Asn 50 | | Val | Pro | Cys | Phe 55 | Leu | Arg | Asp | Trp | Glu 60 | Leu | Gln | Val | His |
| 50 | Phe 65 | _ | Ile | His | Gly | Gln 70 | Gly | Lys | Lys | Asn | Leu 75 | His | Gly | Asp | Gly | Leu 80 |
| 55 | Ala | Ile | Trp | Tyr | Thr 85 | | | | | | | | | | | |
| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 283: | | | | | | | |

| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid |
|----|--|
| 5 | (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 283: |
| | Pro Gly Thr Leu Gln Cys Ser Ala Leu His His Asp Pro Gly Cys Ala 1 5 10 15 |
| 10 | Asn Cys Ser Arg Phe Cys Arg Asp Cys Ser Pro Pro Ala Cys Gln Cys 20 25 30 |
| 15 | |
| | (2) INFORMATION FOR SEQ ID NO: 284: |
| 20 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 27 amino acids (B) TYPE: amino acid |
| 25 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 284: Phe Leu Tyr Asp Val Leu Met Xaa His Glu Ala Val Met Arg Thr His |
| | 1 5 10 15 |
| 30 | Gln Ile Gln Leu Pro Asp Pro Glu Phe Pro Ser 20 25 |
| 35 | (2) INFORMATION FOR SEQ ID NO: 285: |
| | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 6 amino acids(B) TYPE: amino acid(D) TOPOLOGY: linear |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 285: |
| | Gly Trp Tyr Trp Cys Gly 1 5 |
| 45 | (2) INFORMATION FOR SEQ ID NO: 286: |
| | (i) SEQUENCE CHARACTERISTICS: |
| 50 | (A) LENGTH: 129 amino acids(B) TYPE: amino acid(D) TOPOLOGY: linear(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 286: |
| 55 | Met Lys Val Gly Ala Arg Ile Arg Val Lys Met Ser Val Asn Lys Ala 1 5 10 15 |
| 60 | His Pro Val Val Ser Thr His Trp Arg Trp Pro Ala Glu Trp Pro Gln 20 25 30 |

| | Met | Phe | Leu 35 | His | Leu | Ala | Gln | Glu 40 | Pro | Arg | Thr | Glu | Val 45 | Lys | Ser | Arg |
|----|-----------|-----------|------------|------------|-----------|-----------|-------------|-------------------------|------------|------------|-----------|-----------|------------|------------|-----------|-----------|
| 5 | Pro | Leu 50 | Gly | Leu | Ala | Gly | Phe 55 | Ile | Arg | Gln | Asp | Ser 60 | Lys | Thr | Arg | Lys |
| | Pro 65 | Leu | Glu | Gln | Glu | Thr 70 | Ile | Met | Ser | Ala | Ala 75 | Asp | Thr | Ala | Leu | Trp 80 |
| 10 | Pro | Tyr | Gly | His | Gly 85 | Asn | Arg | Glu | His | Gln 90 | Glu | Asn | Glu | Leu | Gln 95 | Lys |
| 15 | Tyr | Leu | Gln | Туг 100 | Lys | Asp | Met | His | Leu 105 | Leu | Asp | Ser | Gly | Gln 110 | Ser | Leu |
| 13 | Gly | His | Thr 115 | His | Thr | Leu | Gln | Gly 120 | Ser | His | Asn | Leu | Thr 125 | Ala | Leu | Asn |
| 20 | Ile | | | | | | | | | | | | | | | |
| | (2) | INF | ∩RMA' | TTON. | FOR | SEO | TD 1 | NO: | 287: | • | | | | | | |
| 25 | (2) | TIVE | | SEQU | ENCE | СНА | RACT | ERIS | TICS | : acid | ls | | | | | |
| 20 | | | | (| (B) T | YPE: | ami OGY: | no a. lin | cid ear | | | • | | | | |
| 30 | | | | | | | | | | EQ I | | | | _ | | |
| | Ser 1 | | His | Lys | Asn 5 | Ser | Val | Ser | GIn | 11e 10 | Ser | Val | Leu | Ser | Gly 15 | Gly |
| 35 | Lys | Ala | Lys | Cys 20 | | Gln | Phe | Cys | Thr 25 | Thr | Gly | Met | Asp | Gly 30 | Gly | Met |
| 40 | Ser | Ile | Trp | | Val | Lys | Ser | Leu 40 | | Ser | Ala | Leu | 45 | | Leu | Lys |
| 40 | Ile | ! | | | | | | | | | | | | | | |
| 45 | (2) | INF | ORMA | MOITA | I FOR | SEÇ |) ID | NO: | 288: | | | | | | | |
| | | | (i) | - | | | | TERIS 21 ar | | S: acio | ds | | | | | |
| 50 | | | (xi) | | (D) | ropoi | LOGY | ino a : lim [PTIC | near | SEQ I | ID NO | D: 28 | 38: | | | |
| 55 | Glu 1 | | ser | . Lys | s Ser | | His | a Ala | Gly | Leu 10 | | Lev | ı Phe | e Ser | Val | |
| | Ala | a Cys | His | Arg | | • | | | | | | | | | | |
| 60 | | | | | | | | | | | | | | | | |

| | (2) INFORMATION FOR SEQ ID NO: 289: |
|------------|---|
| 5 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 289: |
| 10 | Tyr Met Gly Lys Gly Ser Met Thr Gly Leu Ala Leu Lys His Met Phe 1 5 10 15 |
| 15 | Glu Arg Ser Phe Thr 20 |
| | (2) INFORMATION FOR SEQ ID NO: 290: |
| 20 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 27 amino acids(B) TYPE: amino acid(D) TOPOLOGY: linear |
| 25 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 290: |
| 2 0 | Val Thr Gly Ile Ile Asp Ser Leu Thr Ile Ser Pro Lys Ala Ala Arg 1 5 10 15 |
| 30 | Val Gly Leu Leu Gln Tyr Ser Thr Gln Val His 20 25 |
| 25 | (2) INFORMATION FOR SEQ ID NO: 291: |
| 35 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 amino acids (B) TYPE: amino acid |
| 40 | (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 291: |
| | Thr Glu Phe Thr Leu Arg Asn Phe Asn Ser Ala Lys Asp Met Lys Lys 1 5 10 15 |
| 45 | Ala Val Ala His Met Lys Tyr Met 20 |
| 50 | (2) INFORMATION FOR SEQ ID NO: 292: |
| 55 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 27 amino acids(B) TYPE: amino acid(D) TOPOLOGY: linear |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 292: |
| 60 | Gly Lys Gly Ser Met Thr Gly Leu Ala Leu Lys His Met Phe Glu Arg 1 10 15 |

Ser Phe Thr Gln Gly Glu Gly Ala Arg Pro Phe 20 5 (2) INFORMATION FOR SEQ ID NO: 293: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 44 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 293: Ser Thr Arg Val Pro Arg Ala Ala Ile Val Phe Thr Asp Gly Arg Ala 15 Gln Asp Asp Val Ser Glu Trp Ala Ser Lys Ala Lys Ala Asn Gly Ile 25 20 Thr Met Tyr Ala Val Gly Val Gly Lys Ala Ile Glu 40 35 25 (2) INFORMATION FOR SEQ ID NO: 294: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 42 amino acids (B) TYPE: amino acid 30 (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 294: Glu Glu Leu Gln Glu Ile Ala Ser Glu Pro Thr Asn Lys His Leu Phe 35 Tyr Ala Glu Asp Phe Ser Thr Met Asp Glu Ile Ser Glu Lys Leu Lys Lys Gly Ile Cys Glu Ala Leu Glu Asp Ser 40 35 (2) INFORMATION FOR SEQ ID NO: 295: 45 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 11 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 295: Thr Gln Arg Leu Glu Glu Met Thr Gln Arg Met 5

(2) INFORMATION FOR SEQ ID NO: 296:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

| | (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 296: | |
|----|---|---|
| 5 | Pro Gln Gly Cys Pro Glu Gln Pro Leu His 1 5 10 | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 297: | |
| 15 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 297: | |
| 20 | Arg Cys Lys Lys Cys Thr Glu Gly Pro Ile Asp Leu Val Phe Val Ile 1 5 10 15 |) |
| 20 | Asp Gly Ser Lys Ser Leu Gly Glu Glu Asn Phe Glu Val Val Lys Glr 20 25 30 | 1 |
| 25 | Phe | |
| 30 | (2) INFORMATION FOR SEQ ID NO: 298: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 60 amino acids (B) TYPE: amino acid | |
| 35 | (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 298: | |
| | Met Ala Ala Leu Leu Leu Arg His Val Gly Arg His Cys Leu Arg Ala 1 5 10 15 | æ |
| 40 | His Phe Ser Pro Gln Leu Cys Ile Arg Asn Ala Val Pro Leu Gly The 20 25 30 | r |
| | Thr Ala Lys Glu Glu Met Glu Arg Phe Trp Asn Lys Asn Ile Gly Sec. 35 40 45 | r |
| 45 | Asn Arg Pro Leu Ser Pro His Ile Thr Ile Tyr Ser 50 55 60 | |
| 50 | (2) INFORMATION FOR SEQ ID NO: 299: | |
| 55 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 299: | |
| 60 | Val Phe Pro Leu Met Tyr His Thr Trp Asn Gly Ile Arg His Leu Me 1 5 10 15 | t |

Trp Asp Leu Gly Lys Gly Leu Lys Ile Pro Gln Leu Tyr Gln Ser Gly 25 5 10 (2) INFORMATION FOR SEQ ID NO: 300: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 17 amino acids (B) TYPE: amino acid 15 (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 300: Met Ala Ala Leu Leu Leu Arg His Val Gly Arg His Cys Leu Arg Ala 20 His 25 (2) INFORMATION FOR SEQ ID NO: 301: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 18 amino acids 30 (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 301: Val Lys Ser Leu Cys Leu Gly Pro Ala Leu Ile His Thr Ala Lys Phe 35 Ala Leu 40 (2) INFORMATION FOR SEQ ID NO: 302: (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 23 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 302: 50 Val Phe Pro Leu Met Tyr His Thr Trp Asn Gly Ile Arg His Leu Met 5 Trp Asp Leu Gly Lys Gly Leu 20 55 (2) INFORMATION FOR SEQ ID NO: 303: 60 (i) SEQUENCE CHARACTERISTICS:

| _ | (A) LENGTH: 22 amino acids(B) TYPE: amino acid(D) TOPOLOGY: linear(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 303: |
|----|---|
| 5 | Arg Val Trp Asp Val Arg Pro Phe Ala Pro Lys Glu Arg Cys Val Lys 1 5 10 15 |
| 10 | Ile Phe Gln Gly Asn Val 20 |
| 15 | (2) INFORMATION FOR SEQ ID NO: 304: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid |
| 20 | (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 304: |
| | His Asn Phe Glu Lys Asn Leu Leu Arg Cys Ser Trp Ser Pro Asp Gly 1 5 10 15 |
| 25 | Ser Lys Ile Ala Ala Gly Ser Ala Asp Arg Phe Val Tyr Val 20 25 30 |
| 30 | (2) INFORMATION FOR SEQ ID NO: 305: |
| 35 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 305: |
| 40 | Trp Asp Thr Thr Ser Arg Arg Ile Leu Tyr Lys Leu Pro Gly His Ala 1 5 10 10 15 15 15 16 16 17 18 18 18 19 19 19 19 19 19 19 19 19 19 19 19 19 |
| 45 | (2) INFORMATION FOR SEQ ID NO: 306: |
| 50 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 306: |
| 55 | Val Arg Gly Arg Thr Val Leu Arg Pro Gly Leu Asp Ala Glu Pro Glu 1 5 10 15 |
| | Leu Ser Pro Glu 20 |
| 60 | |

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(2) INFORMATION FOR SEQ ID NO: 307:
             (i) SEQUENCE CHARACTERISTICS:
5
                    (A) LENGTH: 19 amino acids
                    (B) TYPE: amino acid
                    (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 307:
10
     Glu Gln Arg Val Leu Glu Arg Lys Leu Lys Lys Glu Arg Lys Lys Glu
                                          10
     Glu Arg Gln
15
      (2) INFORMATION FOR SEQ ID NO: 308:
20
             (i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 13 amino acids
                     (B) TYPE: amino acid
                    (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 308:
25
      Arg Leu Arg Glu Ala Gly Leu Val Ala Gln His Pro Pro
30
      (2) INFORMATION FOR SEQ ID NO: 309:
             (i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 17 amino acids
35
                     (B) TYPE: amino acid
                     (D) TOPOLOGY: linear
             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 309:
      Gly Arg Ile Pro Ala Pro Ala Pro Ser Val Pro Ala Gly Pro Asp Ser
40
                                           10
                       5
      Arg
45
      (2) INFORMATION FOR SEQ ID NO: 310:
              (i) SEQUENCE CHARACTERISTICS:
50
                     (A) LENGTH: 42 amino acids
                     (B) TYPE: amino acid
                     (D) TOPOLOGY: linear
              (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 310:
      Thr Gly Cys Val Leu Val Leu Ser Arg Asn Phe Val Gln Tyr Ala Cys
55
      Phe Gly Leu Phe Gly Ile Ile Ala Leu Gln Thr Ile Ala Tyr Ser Ile
                                                            30
                                        25
60
```

35 5 (2) INFORMATION FOR SEQ ID NO: 311: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 55 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 311: Ser Arg Ser Glu Gly Lys Ser Met Phe Ala Gly Val Pro Thr Met Arg 15 10 Glu Ser Ser Pro Lys Gln Tyr Met Gln Leu Gly Gly Arg Val Leu Leu 20 Val Leu Met Phe Met Thr Leu Leu His Phe Asp Ala Ser Phe Phe Ser 40 Ile Val Gln Asn Ile Val Gly 50 25 (2) INFORMATION FOR SEQ ID NO: 312: 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 60 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 312: 35 Gly Thr Ala Glu Asp Phe Ala Asp Gln Phe Leu Arg Val Thr Lys Gln Tyr Leu Pro His Val Ala Arg Leu Cys Leu Ile Ser Thr Phe Leu Glu 40 Asp Gly Ile Arg Met Trp Phe Gln Trp Ser Glu Gln Arg Asp Tyr Ile 45 Asp Thr Trp Asn Cys Gly Tyr Leu Leu Ala Ser 50 50 (2) INFORMATION FOR SEQ ID NO: 313: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 17 amino acids (B) TYPE: amino acid 55 (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 313: Ala Ser Phe Leu Leu Ser Arg Thr Ser Trp Gly Thr Ala Leu Met Ile 5 10 60

Leu Trp Asp Leu Lys Phe Leu Met Arg Asn

Leu

| 5 | (2) INFORMATION FOR SEQ ID NO: 314: |
|------------|---|
| 10 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 8 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 314: |
| 15 | Leu Met Arg Asn Glu Ser Arg Ser 1 5 |
| 20 | (2) INFORMATION FOR SEQ ID NO: 315: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 13 amino acids (B) TYPE: amino acid |
| 25 | (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 315: |
| 30 | Ala Ser Phe Leu Leu Ser Arg Thr Ser Trp Gly Thr Ala 1 5 10 |
| | (2) INFORMATION FOR SEQ ID NO: 316: |
| 35 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 316: |
| 40 | Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met 1 5 10 15 |
| 45 | Met Ser Ser Phe 20 |
| | (2) INFORMATION FOR SEQ ID NO: 317: |
| 50 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 27 amino acids(B) TYPE: amino acid(D) TOPOLOGY: linear |
| <i>5 5</i> | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 317: |
| 55 | Asp Pro Arg Arg Pro Asn Lys Val Leu Arg Tyr Lys Pro Pro Pro Ser 1 5 10 15 |
| 60 | Glu Cys Asn Pro Ala Leu Asp Asp Pro Thr Pro 20 25 |

| 5 | (2) | INF | ORMA! | rion | FOR | SEQ | ID 1 | 10: 3 | 18: | | | | | | | |
|----|----------|-----------|-------------|-----------|----------------------|-----------------------|---------------------|---------------------------------|---------------------|-----------|------|-------|------------|-----------|-----------|-----|
| , | | | (i) | (1 | A) L B) T | ENGT YPE : | H: 3 ami: | ERIST 0 am: no ac line | ino a cid | | 5 | | | | | |
| 10 | | | (xi) | SEQU | | | | | | EQ I | D NO | : 31 | B : | | | |
| | Asp 1 | Tyr | Met | Asn | Leu 5 | Leu | Gly | Met | Ile | Phe 10 | Ser | Met | Cys | Gly | Leu 15 | Met |
| 15 | Leu | Lys | Leu | Lys 20 | Trp | Cys | Ala | Trp | Val 25 | Ala | Val | Tyr | Cys | Ser 30 | | |
| 20 | (2) | INF | ORMA' | rion | FOR | SEQ | ID I | 10: 3 | 319: | | | | | | | |
| 25 | | | | (| A) L B) T D) T | ENGT YPE: OPOL | H: 2 ami OGY: | 2 am no a lin | ino a cid ear | acid | | : 319 | 9∶ | | | |
| 30 | Met 1 | Leu | Ser | Ile | Ser 5 | Ala | Val | Val | Met | Ser 10 | Tyr | Leu | Gln | Asn | Pro 15 | Gln |
| | Pro | Met | Thr | Pro 20 | Pro | Trp | | | | | | | | | | |
| 35 | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 320: | | | | | | | |
| 40 | | | | (| A) L B) T D) T | ENGT YPE : OPOL | H: 5 ami OGY: | 2 am no a lin | ino cid ear | acid | | : 32 | 0: | | | |
| 45 | Ala 1 | Ala | Gly | Asp | Gly 5 | | Val | Lys | Leu | Gly 10 | Thr | Leu | Gly | Ser | Gly 15 | Ser |
| | Glu | Ser | Ser | Asn 20 | Asp | Gly | Gly | Ser | Glu 25 | Ser | Pro | Gly | Asp | Ala 30 | Gly | Ala |
| 50 | Ala | Ala | . Xaa 35 | Gly | Gly | Gly | Trp | Ala 40 | Ala | Ala | Ala | Leu | Ala 45 | Leu | Leu | Thr |
| 55 | Gly | Gly 50 | _ | Glu | | | | | | | | | | | | |
| | (2) | INE | ORMA | MOITA | FOF | R SEÇ |) ID | NO: | 321: | 1 | | | | | | |
| 60 | | | (i) | SEQU | ENCE | CHA | RACT | ERIS | TICS | : | | | | | | |

| | | | (xi) | (1 | B) T | PE: | amin OGY: | 77 an no ao line PTION | cid ear | | | : 32: | L: | | | |
|----|------------|------------|-------------|-------------|----------------|------------|----------------|---------------------------------|-------------|------------|------------|------------|------------|------------|--------------------|------------|
| 5 | Ala 1 | Ala | Asp | Asn | Tyr 5 | Gly | Ile | Pro | Arg | Ala 10 | Cys | Arg | Asn | Ser | Ala 15 | Arg |
| 10 | Ser | Tyr | Gly | Ala 20 | Ala | Trp | Leu | Leu | Leu 25 | Xaa | Pro | Ala | Gly | Ser 30 | Ser | Arg |
| | Val | Glu | Pro 35 | Thr | Gln | Asp | Ile | Ser 40 | Ile | Ser | Asp | Gln | Leu 45 | Gly | Gly | Gln |
| 15 | Asp | Val 50 | Pro | Val | Phe | Arg | Asn 55 | Leu | Ser | Leu | Leu | Val 60 | Val | Gly | Val | Gly |
| 20 | Ala 65 | Val | Phe | Ser | Leu | Leu 70 | Phe | His | Leu | Gly | Thr 75 | Arg | Glu | Arg | Arg | Arg 80 |
| 20 | Pro | His | Ala | Xaa | Glu 85 | Pro | Gly | Glu | His | Thr 90 | Pro | Leu | Leu | Ala | Pro 95 | Ala |
| 25 | Thr | Ala | Gln | Pro 100 | Leu | Leu | Leu | Trp | Lys 105 | His | Trp | Leu | Arg | Glu 110 | Xaa | Ala |
| | Phe | Tyr | Gln 115 | Val | Gly | Ile | Leu | Tyr 120 | Met | Thr | Thr | Arg | Leu 125 | Ile | Val | Asn |
| 30 | Leu | Ser 130 | | Thr | Tyr | Met | Ala 135 | Met | Tyr | Leu | Thr | Tyr 140 | Ser | Leu | His | Leu |
| 35 | Pro 145 | _ | Lys | Phe | Ile | Ala 150 | Thr | Ile | Pro | Leu | Val 155 | Met | Tyr | Leu | Ser | Gly 160 |
| | Phe | Leu | Ser | Ser | Phe 165 | Leu | Met | Lys | Pro | 11e 170 | Asn | Lys | Cys | Ile | Gly 17 5 | Arg |
| 40 | Asn | | | | | | | | | | | | | | | |
| | (2) | INF | 'ORMA | TION | FOR | SEQ | ID | NO: | 322: | | | | | | | |
| 45 | | | (i) | (| (A) I (B) I | ENGT | TH: 2 : ami | ERIS 243 a ino a : lir | mino cid | | ids | | | | | |
| 50 | | | (xi) | | | | | PTIC | | EQ I | D NO |): 32 | 22: | | | |
| | Arg 1 | | Thr | Asp | Asn 5 | | Glu | Gly | Lys | Trp | | Gly | Arg | Thr | Ala 15 | |
| 55 | Gly | ser Ser | Tyr | : Gly 20 | | Ile | . Lys | Thr | Thr 25 | | Val | . Glu | ılle | Xaa 30 | | Asp |
| | Ser | : Leu | ı Lys 35 | | Lys | Lys | a Asp | Ser 40 | | Gly | Ala | Pro | Ser 45 | | Pro | Ile |
| 60 | Glu | ı Asp |) Asp | Glr | Glu | (Val | Туг | Asp | Asp | Val | Ala | a Glu | ı Gln | Asp | Asp | Ile |

| | | 50 | | | | | 55 | | | | | 60 | | | | |
|----|------------|------------|------------|--------------|------------|---------------|------------|------------|---------------|------------|------------|-----------------|-------------|------------|------------|------------|
| 5 | Ser 65 | Ser | His | Ser | Gln | Ser 70 | Gly | Ser | Gly | Gly | Ile 75 | Phe | Pro | Pro | Pro | Pro 80 |
| 3 | Asp | Asp | Asp | Ile | Tyr 85 | Asp | Gly | Ile | Glu | Glu 90 | Glu | Asp | Ala | Asp | Asp 95 | Gly |
| 10 | Phe | Pro | Ala | Pro 100 | Pro | Lys | Gln | Leu | Asp 105 | Met | Gly | Asp | Glu | Val 110 | Tyr | Asp |
| | Asp | Val | Asp 115 | Thr | Ser | Asp | Phe | Pro 120 | Val | Ser | Ser | Ala | Glu 125 | Met | Ser | Gln |
| 15 | Gly | Thr 130 | Asn | Val | Gly | Lys | Ala 135 | Lys | Thr | Glu | Glu | Lys 140 | Asp | Leu | Lys | Lys |
| 20 | Leu 145 | Lys | Lys | Gln | Xaa | Lys 150 | Glu | Xaa | Lys | Asp | Phe 155 | Arg | Lys | Lys | Phe | Lys 160 |
| 20 | Tyr | Asp | Gly | Glu | Ile 165 | Arg | Val | Leu | Tyr | Ser 170 | Thr | Lys | Val | Thr | Thr 175 | Ser |
| 25 | Ile | Thr | Ser | Lys 180 | Lys | Trp | Gly | Thr | Arg 185 | Asp | Leu | Gln | Val | Lys 190 | Pro | Gly |
| | Glu | Ser | Leu 195 | Glu | Val | Ile | Gln | Thr 200 | Thr | Asp | Asp | Thr | Lys 205 | Val | Leu | Cys |
| 30 | Arg | Asn 210 | | Glu | Gly | Lys | Tyr 215 | Gly | Tyr | Val | Leu | Arg 220 | Ser | Tyr | Leu | Ala |
| 35 | Asp 225 | Asn | Asp | Gly | Glu | Ile 230 | | Asp | Asp | Ile | Ala 235 | | Gly | Cys | Ile | Tyr 240 |
| 55 | Asp | Asn | Asp | | | | | | | | | | | | | |
| 40 | (2) | INF | ORMA | TION SEOU | | | | | | 3 <i>•</i> | | | | | | |
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| 50 | Ser 1 | | : Ser | Ala | Leu 5 | | Arg | Leu | ı Ala | Ser 10 | | Ala | a Arg | Val | Gly 15 | |
| 30 | Arg | , Lei | ı Phe | Arg 20 | | : Gly | Cys | : Ala | Arg 25 | | Ala | Gl _y | / Asp | Gly 30 | | Val |
| 55 | Arg | y His | s Ala | | Gly | / Gly | / Val | His | | e Glu | ı Pro | Arg | 7 Tyr 45 | | Glr | Phe |
| | Pro | Glr 50 | | ı Thi | : Arg | g Sei | Glr Si | | L Phe | e Glr | ı Sei | Glu 60 | ı Ph∈ | e Phe | e Ser | Gly |
| 60 | Lev | ı Me | t Trị | p Phe | e Tr | o Ile | e Lei | ı Tr | o Arg | g Phe | e Trį | o His | s Asp | Sei | Glu | ı Glı |

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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

| | ns made below relate to the microorgan 73 . lii | |
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| B. IDENTIFIC | CATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of deposita | ury institution American Type Cù | olture Collection |
| 10801 Univers | ginia 20110-2209 | and country) |
| Date of deposit | March 7, 1997 | Accession Number 97923 |
| | NAL INDICATIONS (leave blank if r | This information is continued on an additional sheet |
| | | ONS (leave blank if not applicable) ternational Bureau later (specify the general nature of the indications, e.g., "Accession |
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BNSDOCID: <WO 9842738A1_IA>

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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

| A. The indications made below relate to the microorganism refer on page 73 . line N/ | |
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| B. IDENTIFICATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of depositary institution American Type Culture Co | ollection |
| Address of depositary institution (including postal code and coun 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | (יבְיזוּ |
| Date of deposit May 22, 1997 | Accession Number 209071 |
| C. ADDITIONAL INDICATIONS (leave blank if not applice | able) This information is continued on an additional sheet |
| D. DESIGNATED STATES FOR WHICH INDICATION | ONS ARE MADE (if the indications are not for all designated States) |
| E. SEPARATE FURNISHING OF INDICATIONS (lear | ve blank if not applicable) |
| The indications listed below will be submitted to the International Number of Deposit") | al Burcau later (specify the general nature of the indications, e.g., "Accession |
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(PCT Rule 13bis)

| A. The indications made below ron page 73 | elate to the microorganism refer | |
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| B. IDENTIFICATION OF D | EPOSIT | Further deposits are identified on an additional sheet |
| Name of depositary institution | American Type Culture Co | ollection |
| Address of depositary institution (10801 University Boulevard Manassas. Virginia 20110-220 United States of America | | ntry) |
| Date of deposit February 25, | 1998 | Accession Number 209641 |
| C. ADDITIONAL INDICA | FIONS (leave blank if not applic | rable) This information is continued on an additional sheet |
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| D. DESIGNATED STATES | FOR WHICH INDICATION | ONS ARE MADE (if the indications are not for all designated States) |
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

| A. The indications made below relate to the microorg on page 75 | ganism referred to in the description . line N/A |
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| B. IDENTIFICATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of depositary institution American Type | Culture Collection |
| Address of depositary institution (including postal con 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | de and country) |
| Date of deposit July 24, 1997 | Accession Number 209179 |
| C. ADDITIONAL INDICATIONS (leave blank | if not applicable) This information is continued on an additional sheet |
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| D. DESIGNATED STATES FOR WHICH IN | NDICATIONS ARE MADE (if the indications are not for all designated States) |
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| E. SEPARATE FURNISHING OF INDICAT | CIONS (leave blank if not applicable) |
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| | ns made below relate to the microorga 77 | anism referred to in the description line N/A |
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| B. IDENTIFIC | ATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of deposita | ry institution American Type C | Culture Collection |
| 10801 Universi | inia 20110-2209 | e and country) |
| United States C | America | |
| Date of deposit | March 7, 1997 | Accession Number 97924 |
| C. ADDITION | NAL INDICATIONS (leave blank if | f not applicable) This information is continued on an additional sheet |
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

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| | ns made below rel | | nism referred ine N/A | to in the description |
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| | CATION OF DE | POSIT | | Further deposits are identified on an additional sheet |
| Name of deposita | ry institution | American Type Cu | ulture Colle | |
| 10801 Universi | ity Boulevard ginia 20110-220 | ncluding postal code 9 | and country | ·) |
| Date of deposit | March 13, 199 | 7 | , | Accession Number 97958 |
| C. ADDITIO | NAL INDICATI | IONS (leave blank if i | not applicable | This information is continued on an additional sheet |
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| A. The indications made below relate to the microorganism on page 80 . line | n referred to in the description N/A |
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| B. IDENTIFICATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of depositary institution American Type Cultu | re Collection |
| Address of depositary institution (including postal code and 10801 University Boulevard | d country) |
| Manassas, Virginia 20110-2209 United States of America | |
| Date of deposit May 22, 1997 | Accession Number 209072 |
| C. ADDITIONAL INDICATIONS (leave blank if not | applicable) This information is continued on an additional sheet |
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| D. DESIGNATED STATES FOR WHICH INDIC | ATIONS ARE MADE (if the indications are not for all designated States) |
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| . IDENTIFIC | CATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of deposita | ry institution American Ty | Type Culture Collection |
| Address of depos | sitary institution (including poste | al code and country) |
| Manassas. Virg United States o | inia 20110-2209 | |
| Date of deposit | September 4, 1997 | Accession Number 209235 |
| C. ADDITIO | NAL INDICATIONS (leave b | blank if not applicable) This information is continued on an additional sheet |
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| A. The indications made below relate to the microorganism on page 84 . iine | referred to in the description N/A |
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| B. IDENTIFICATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of depositary institution American Type Cultur | re Collection |
| Address of depositary institution (including postal code and 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | d country) |
| Date of deposit August 28, 1997 | Accession Number 209226 |
| C. ADDITIONAL INDICATIONS (leave blank if not a | applicable) This information is continued on an additional sheet |
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| D. DESIGNATED STATES FOR WHICH INDIC. | ATIONS ARE MADE (if the indications are not for all designated States) |
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| E. SEPARATE FURNISHING OF INDICATIONS The indications listed below will be submitted to the International Company of Deposit") | S (leave blank if not applicable) ational Bureau later (specify the general nature of the indications, e.g., "Accession of the indications of the indication of th |
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

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| A. The indications made below relate to the microorganism on page 84 | referred to in the description N/A |
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| B. IDENTIFICATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of depositary institution American Type Culture | re Collection |
| Address of depositary institution (<i>including postal code and</i> 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | country) |
| Date of deposit March 13, 1997 | Accession Number 97957 |
| C. ADDITIONAL INDICATIONS (leave blank if not ap | pplicable) This information is continued on an additional sheet |
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| D. DESIGNATED STATES FOR WHICH INDICA | ATIONS ARE MADE (if the indications are not for all designated States) |
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| E. SEPARATE FURNISHING OF INDICATIONS | |
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| A. The indications made below relate to the microorganism refer on page 84 , line N/A | 1 |
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| B. IDENTIFICATION OF DEPOSIT | Further deposits are identified on an additional sheet |
| Name of depositary institution American Type Culture Co | ollection |
| Address of depositary institution (including postal code and cour | ntry) |
| 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | |
| Date of deposit May 22, 1997 | Accession Number 209073 |
| C. ADDITIONAL INDICATIONS (leave blank if not application) | cable) This information is continued on an additional sheet |
| D. DESIGNATED STATES FOR WHICH INDICATION | ONS ARE MADE (if the indications are not for all designated States) |
| E. SEPARATE FURNISHING OF INDICATIONS (lea | ave blank if not applicable) |
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What Is Claimed Is:

- 1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
- (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
- (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
- (c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
- (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
- (e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X, having biological activity;
 - (f) a polynucleotide which is a variant of SEQ ID NO:X;
 - (g) a polynucleotide which is an allelic variant of SEQ ID NO:X;
 - (h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
- (i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
- 2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.
- 3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

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4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

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5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

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- 6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
- 7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
 - 8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

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- 9. A recombinant host cell produced by the method of claim 8.
- 10. The recombinant host cell of claim 9 comprising vector sequences.
- 11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z, having biological activity;

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- (c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
- (d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
- (e) a secreted form of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
- (f) a full length protein of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

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- (g) a variant of SEQ ID NO:Y;
- (h) an allelic variant of SEQ ID NO:Y; or
- (i) a species homologue of the SEQ ID NO:Y.
- 12. The isolated polypeptide of claim 11, wherein the secreted form or the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
 - 13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.
 - 14. A recombinant host cell that expresses the isolated polypeptide of claim 11.
 - 15. A method of making an isolated polypeptide comprising:
 - (a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and
 - (b) recovering said polypeptide.
 - 16. The polypeptide produced by claim 15.
 - 17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.
 - 18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
 - (a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and
 - (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.
 - 19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
 - (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and
 - (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

- 20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:
 - (a) contacting the polypeptide of claim 11 with a binding partner; and
- 5 (b) determining whether the binding partner effects an activity of the polypeptide.
 - 21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
- 10 22. A method of identifying an activity in a biological assay, wherein the method comprises:
 - (a) expressing SEQ ID NO:X in a cell;
 - (b) isolating the supernatant;
 - (c) detecting an activity in a biological assay; and
 - (d) identifying the protein in the supernatant having the activity.
 - 23. The product produced by the method of claim 22.

PCT/US 98/05311

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C12N5/10 C07K14/47 C07K16/18 C12N1/21 G01N33/53 G01N33/50 A61K38/17 G01N33/68 C1201/68 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12N C07K C12Q G01N IPC 6 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Category ' L. HILLIER ET AL.: "The WashU-Merck EST 1-3, X 7-11,21 project" EMBL SEQUENCE DATABASE, 2 July 1995, HEIDELBERG, FRG, XP002068365 y187a06.rl Homo sapiens cDNA clone 44938 5': Accession no. H08241; L. HILLIER ET AL.: 1-3, 7-11,21 "The "WashU-Merck EST X project" EMBL SEQUENCE DATABASE, 26 August 1995, HEIDELBERG, FRG, XP002068366 ym94e01.rl Homo sapiens cDNA clone 166584 5'. Accession no. R88485; 1 - 23WO 97 07198 A (GENETICS INSTITUT) 27 Α February 1997 see the whole document -/--Further documents are listed in the continuation of box C. Patent family members are listed in annex. Х Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docudocument referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means in the art. document published prior to the international filing date but "&" document member of the same patent family later than the priority date claimed Date of mailing of the international search report Date of the actual completion of the international search 16, 09, 1998 17 June 1998 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 HORNIG H.

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Inte .ional application No.

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| Box i | Observations where certain claims were found unsoarchable (Continual) in of it in a finist sheety |
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| This Inte | rnational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: |
| 1. X | Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although claim 17 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. |
| 2. | Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| 3. | Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box II | Observations where unity of invention is lacking (Continuation of item 2 of first sheet) |
| | ernational Searching Authority found multiple inventions in this international application, as follows: |
| se | e further information sheet |
| | |
| 1. | As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. |
| 2 | As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. |
| 3. | As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: |
| 4. X | No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: see further information sheet |
| Remark | The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees. |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1. Claims: (1-23) partially

-An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from SEQ ID no. 11; wherein said polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein encoding the sequence SEQ ID no.125 or the polypeptide encoded by the cDNA sequence included in ATCC Deposit nos: 97923/209071 , which is hybridizable to SEQ ID no.11; a recombinant vector comprising said isolated nucleic acid molecule; a method of making a recombinant host cell comprising said isolated nucleic acid molecule; a recombinant host cell comprising said vector; an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence SEQ ID no. 125; an isolated antibody that binds specifically to said isolated polyeptitde; a recombinant host cell that expresses said isolated polypeptide; a method of making said polypeptide; a method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of said polypeptide; a method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject using said polynucleotide and/or polypeptide sequence; a method for identifying a binding partner to said polypeptide; a gene corresponding to the cDNA sequence of SEQ ID no.11; a method for identifying an activity in a biological assay, by using the expression of SEQ ID no. 125;

Inventions 2 to 87. Claims: (12-23) partially

-Idem as subject 1 but limited to gene nos. 2 to 87 respectively cDNA clone sequences HAGFY16/HBMCF37/HFLQB16 to HCED021. (Invention 2 is limited to SEQ ID nos. 12,98,99,126,212 and 213; Invention 3 is limited to SEQ ID nos.13 and 127;; Invention 87 is limited to SEQ ID nos.97 and 211;)

nt ation on patent family members

International Application No
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